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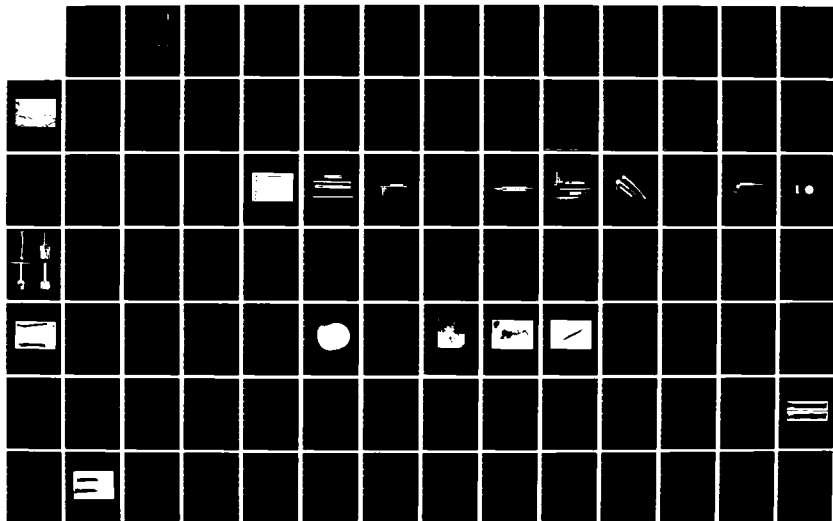
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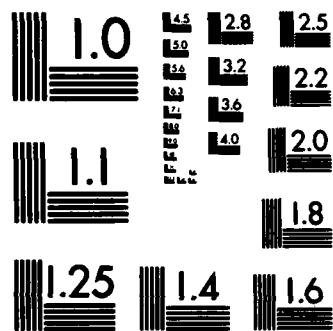
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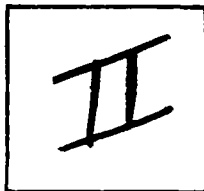


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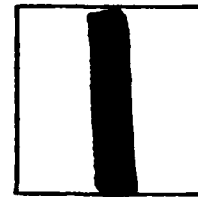
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INTERNAL PROSTHETIC REPLACEMENT OF SKELETAL SEGMENTS
LOST IN COMBAT RELATED INJURIES

Final Report

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August 1981

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Segmented prosthetic replacements for the tibia, femur, humerus of adult baboons were successfully employed in studies involving times from a few weeks to several years. These devices utilized porous titanium composite in association with load-bearing components to replace large bone defects artificially created. The objective was to evaluate the potential for bone ingrowth into the porosity to provide fixation and ultimately to invest the prosthetic device in a load-bearing system involving the residual bone		

extremities. Clinical studies of the long bone reconstructions are presented. The prosthetic devices were designed and produced for this research program. There were corollary studies on the biocompatibility of titanium and other metals used for load-bearing implantable devices.

FOREWORD

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23, Revised 1978).

For the protection of human subjects the investigator(s) have adhered to policies of applicable Federal Law 45CFR46.

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PREFACE

This is a final report summarizing a program of research which began in June 1971 and continued until March 1979.

The general objectives of this program were to develop prostheses and clinical techniques which would permit reconstruction of major segments of a long bone and restore it to reasonably normal function. A further objective was to determine whether the growing bony tissue would utilize the porous nature of the special prosthetic material to remodel the long bone. The program involved clinical studies, design, development and prototype construction of prostheses and implantation tooling and, finally, proof of performance under conditions of implantation.

Many of the results of this program have appeared as publications in the professional literature. These have been edited into the body of this report and reference to the original publication is made at the appropriate point.

I. INTRODUCTION

It is well established experimentally (1-12) that connective tissue and, more particularly, calcified tissue will penetrate into and along the pore channels of a porous material. The material itself may be metallic, ceramic or polymeric provided that the matrix is inert under in vivo conditions.

Various materials and several processes for producing porous aggregates have been used. Most of these processes are involved with sintering or combinations of pressure and sintering. A transient or stable liquid phase is involved in some. In the latter case, the liquid phase is continuous and the porosity is generated by leaching out that phase.

Porous solids derived from powders generally require the use of fine particles to achieve adequate interparticle bonding in reasonable time at elevated temperatures. Such solids are often very fragile unless protracted sintering treatments are applied; in which case, much of the porosity ceases to be interconnecting with the result that tissue ingrowth is not much more than superficial.

The mechanical properties of sintered powders are not very propitious. Porous ceramics especially are very weak and brittle. Cracks will propagate quickly throughout the whole body of the porous aggregate at low stresses or with small impact energies. Consolidated metal powders with porosities in the range of 40-60% void content are stronger but still very brittle. For both sintered ceramic and metal powders, compliances are not more than twice the dense equivalent and, in any case, much smaller than bone.

A porous metallic material made by molding and sintering short-length, kinked fibers has been the basis for the present development of new prosthetic devices which achieve both fixation and investment by newly growing calcified tissue. This porous material has some valuable attributes for these applications. At about 50%

void content, the pore channels are interconnecting. This is especially important when the porous material is intended as a basis for bone remodelling. The pore sizes are governed largely by the diameter of the wire or fiber used. The pore shapes are nonsymmetrical as may be seen in Figure 1. Inscribed circles provide basis for description of voids. These generate pore dimensions or openings in the range of 200-400 microns which is well within the range cited (13) as conducive to bone invasion.

Components such as thin sleeves can be molded from short-length fibers to close tolerances. Tolerances can be maintained from part to part so that it is possible to consider the manufacture of components of precise and reproducible dimensions. This is important because the selective ingrowth of bony tissue over large areas of interface requires zero clearance or slightly negative clearance to the resected or excavated site. Violation of this prerequisite will cause the preferential ingrowth of fibrous tissue which precludes the bony tissue.

The porous aggregate manufactured from wire or fiber cannot fail mechanically by the propagation of a crack. Failure occurs over a large distortion range by a tearing action much the same as a fabric, but in fact, represents the progressive rupture of the sintered bonds between fibers.

The compliance of this porous material is larger than cortical bone itself. Thus when hosted in a bony matrix it behaves much as bone elastically; in particular, it distributes applied force as would a cancellous bone.

While any metallic material can be used, the present work has utilized titanium wire almost exclusively. There are a number of reasons for this. Titanium has an excellent record of biocompatibility. It is available as a very soft and deformable, high purity metal which is well suited to the molding operations. It sinters with the formation of very strong bonds at reasonable temperatures. Both unalloyed and high strength alloys can be forged, machined and welded without difficulty.



Figure 1 Nonsymmetrical pore shapes.

The objectives of this extended research program were to demonstrate the functional feasibility of reconstructing long bones from which segments have been lost through trauma or the necessity to resect because of trauma or disease. In either event, the objective would be to reconstitute the residual fragments with a prosthesis component that would permit permanent attachment and ultimate remodelling while allowing early restoration of the limb function.

During the period of attachment and remodelling, the limb should be load-bearing. While the porous material has appreciable strength, it could not sustain large dynamic body forces. Accordingly, a segment reconstruction prosthesis must be a composite construction which utilizes both solid metal, high strength components and porous metal disposed strategically to provide the bony ingrowth while not sustaining large stresses.

With these separate functions of the components in mind, there is clearly a strong design and manufacturing development feature to the research program. It has been the intent to design devices which can be manufactured by methods which utilize present state of the art. It has also been a basic philosophy that, while a custom fabrication feature must be accepted, the design and manufacturing approaches can be sufficiently simplified that rapid response to demand is possible or alternatively immediate access is feasible by establishment of an inventory scheme.

II. POROUS TITANIUM

A metallic material with a wide but controlled range of interconnecting porosity can be made from wire by a series of simple process steps. Short lengths of wire can be molded and consolidated in a tooling system that involves a die (split or not) and opposing punches. The wire pieces are trapped in the space defined by the die-punch assembly. The motion of punches forces the wire pieces together so that they

fill space, interlock mechanically and acquire a bulk shape defined by the die and punch face profiles. The generation of suitable porosity while this consolidation step proceeds is governed by the preliminary shape of the wire pieces and by the method of loading into the die cavity. The wire is kinked in the form of a repeated sine wave type pattern before cutting to length. The kinked wire is charged into the die cavity in twisted groups and, as much as possible, with the wire axis vertical. All of these precautions create an initial condition whereby as the punches move the wire pieces buckle, interlock and compress in a very random motion. The result is a uniform distribution of interconnecting pores. The volume of porosity can be varied from 60-40% with 50% preferred. Higher void volumes are possible but the pieces are difficult to handle.

The molded piece may be removed from the die-punch assembly without difficulty. The piece itself has considerable strength quite sufficient for handling. The piece has a desired shape and dimensions close to intended. The complete process allows the manufacture of parts to close tolerances. In the as-molded state the wire pieces are interlocked in complex and random fashion within the confines of the shape. Inside the body the wires are touching at many points.

The second step of the process involves a high temperature bonding process called sintering. The conditions for sintering involve temperatures of about 1200°C for times of 2-3 hours in a vacuum of 10^{-6} torr. By the sintering operation all points of contact become bonds with an actual bridge of metal formed although there is no fusion and the temperatures are below melting points. The process of sintering creates bonds or welds between touching metals (and between ceramics also) and it slowly eliminates the voids. It is theoretically possible to eliminate all voids by sintering. However, in the present process sintering is used only to create metal bonds between touching wires. After sintering the formed shape has changed somewhat in dimensions but is mechanically much stronger. It is also much softer because

of recrystallization.

The third step of the process is to return the sintered part to the die-punch assembly and re-size it for purposes only of shape and dimensional control. If there is any uncertainty about integrity, resintering and resizing can be done but this is rarely necessary.

The process is applicable to any metal available in wire form, such as wrought Co-Cr-W alloy, 316 stainless steel and titanium (alloys). We have chosen to work exclusively with titanium and its alloys for several good reasons. Titanium embraces soft metals and a series of strong alloys. Yield strengths can range from 30,000-180,000 psi. Alloyed and unalloyed materials are free of couple corrosion so that designs can incorporate soft materials for good formability and strong materials for service load endurance. Titanium can be formed, machined and welded quite easily. The soft titanium wire molds more easily than the Co-Cr and stainless steels and provides stronger sintered bonds. There is no evidence that porous titanium suffers from crevice corrosion - which is certainly a basis for ruling out porous stainless steel. While we have used titanium predominantly, we have also manufactured prostheses from Co-Cr-W wire and Co-Cr-Mo castings.

The fourth step in the process is an assembly of porous-shaped parts with solid formed or machined parts. In general the approach to design is to surface with the porous material on a solid or tubular object which is of solid titanium and strong enough to withstand the service forces in vivo. The fixation of the porous to the solid titanium can be accomplished by one or both of two approaches. Sleeves of porous metal can be fitted on a solid and captured between solid ends welded in position later. The sleeves or plate-like inserts can be sinter bonded to a solid substrate. Sleeves can be fixed against linear motion these ways. They can also be fixed against rotation motion by molding flats on the inside profile that match flats machined on the curved solid surfaces. With the recent acquisition of a large

high temperature, vacuum furnace all finished assemblies are given a 1250°C sinter as the finishing operation.

The porous material has some unusual mechanical property attributes which have been presented in a published paper entitled, "Some Mechanical Properties of Sintered Fiber Metal Composites" by W. Rostoker, J.O. Galante and G. Shen which appeared in the Journal of Testing and Evaluation (ASTM), 2, 1974, 107-112. Portions of this manuscript follow.

This paper presents a quantitative appraisal of the mechanical properties of molded and sintered fiber composites and the factors which are influential. Most of the present work has been on the elastic properties. A more limited study of tensile strength was also made.

Materials and Methods

Unalloyed, annealed titanium and annealed Vitallium* wires were used in these studies. The wire was converted to fiber form first by kinking between meshing gears and second by cutting into appropriate lengths. Wire diameters ranged from 0.19 to 0.3 mm. Preweighed amounts of fiber were charged into dies and molded by piston motion using essentially conventional powder metallurgy techniques without lubricants. Great care was taken to insure that the piston faces were parallel.

The "green" molded shape can be readily handled. The composite is coherent essentially because of very complex mechanical interlock which is rendered more effective by the kinking preparation. When subjected to a vacuum heat treatment at elevated temperatures, the metal is recrystallized and points of contact in the composite become sintered bonds. There is some spring back associated with the original molding operation. Better conformity to the die dimensions are attained by repressing or coining the same die.

*Wrought Co-19/21% Cr-14/16% W alloy manufactured by Howmedica, Inc., Rutherford, New Jersey.

Elastic behavior was studied primarily by the compression of simple, right-cylindrical shapes having approximate dimensions: 13 mm diameter by 13 mm high. For this shape the wire was cut to lengths of about 20 mm. Bend tests and tensile tests were performed on molded bars having dimensions: 50 mm long x 9.5 mm wide x 4 mm thick. Fiber lengths in this case were about 50 mm in length.

Compression testing was performed using the drive system of an Instron universal testing machine. A special die set was constructed that provided good axial alignment and parallelism of platens. This die set was placed between the platens of the Instron machine. The upper punch in contact with the test specimen contained its own load cell. Relative motion during testing was monitored by a Baldwin MRI extensometer, for compression, and a sensitive linear variable differential transformer transducer, for bending, coupled to the punches. The arrangement is illustrated diagrammatically in Figure 2. The outputs of the load cell and extensometer were automatically plotted by the X-Y recorder of the Instron machine. By a variation of this arrangement, testing in three-point bending was accomplished.

Tensile testing of molded flat bars was accomplished using friction grips leaving a gage section of about 25 mm.

The elastic behavior was examined by a loading-unloading procedure with successively higher maximum loads. As long as the loading and unloading curves provided a closed loop, the material was judged to be in the elastic regime. The stress-strain curves in the elastic range were nonlinear having a form illustrated in Figure 3 which is similar to elastomeric materials but with a smaller elastic strain range. For purposes of characterization, these curves were approximated as two straight lines whose slopes were designated as the elastic moduli in the low strain regime and in the high strain regime, respectively.

The following variables were permuted into the manufacture of test specimens to evaluate their influence on elastic properties. There was less comprehensive

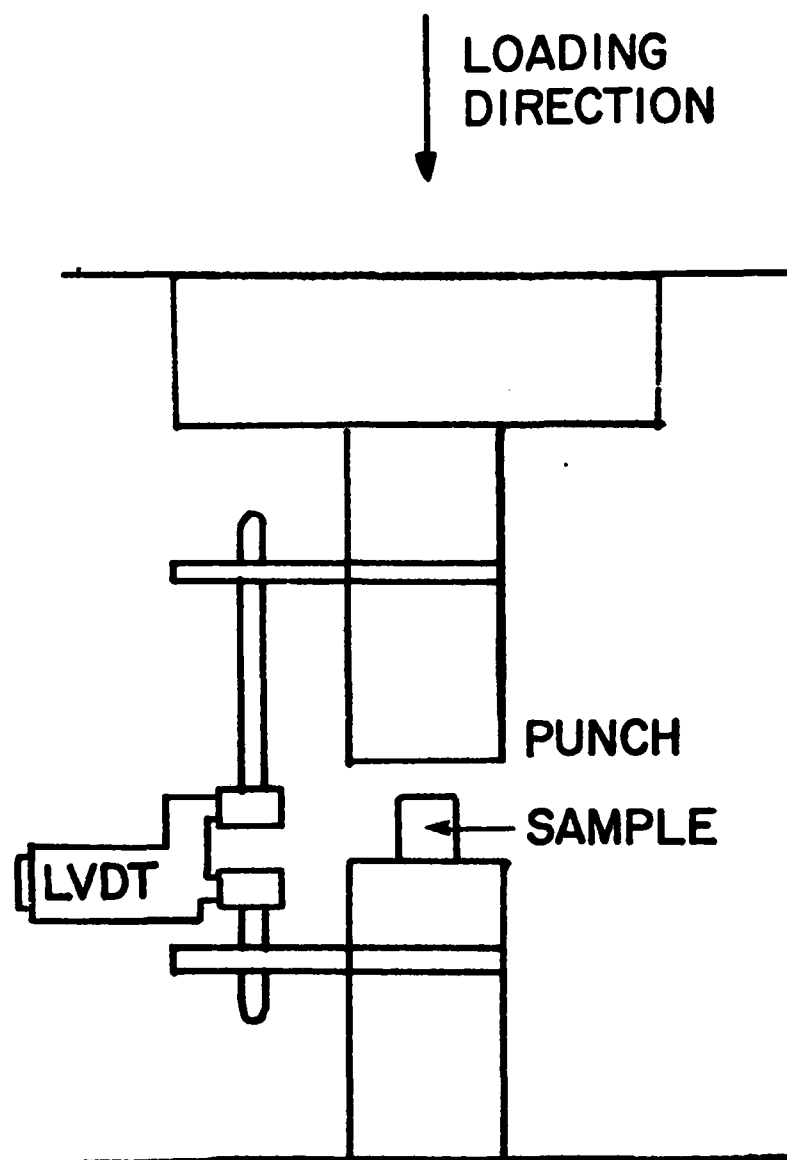


Figure 2

Diagrammatic arrangement of the compression test system.

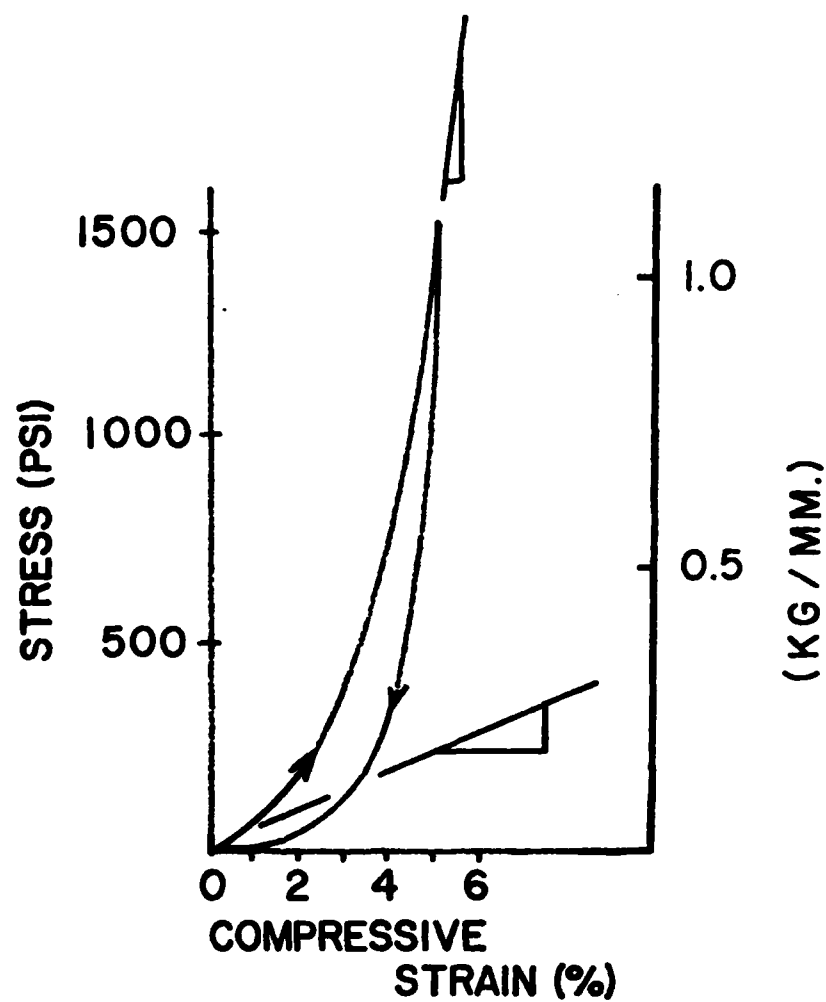


Figure 3

Typical reversible stress-strain diagram of elastic behavior showing the limiting elastic moduli in the low strain and high strain regimes.

evaluation of effects on tensile strength and elongation.

- Void content in the range 30 - 60%
- Wire diameters of 0.225, 0.30 mm (Vitalium) and 0.19, 0.25 and 0.30 mm (titanium)
- Sintering temperatures ranging from 1100-1300°C

Sintering times were held constant at 3 hours and the sintering vacuum operated at 10^{-7} torr. The range of void contents represents practical limits. At the lower limit there is poor "green" strength and dimensional control and at the upper limit the pore sizes become too small for tissue invasion. The wire diameters also represent a practical range of choices. There are difficulties with charging into die orifices and in molding with wire sizes which are smaller or larger in diameter.

Experimental Results

Using bend deflection measurements and beam load-deflection elastic equations, an elastic modulus can be calculated. There is some uncertainty whether beam equations can be applied to a high porous composite. Moreover, examination of the specimens indicated small indentations at the points of loading and support which would represent corrections to the deflection of an indeterminate nature. However, the calculated elastic moduli, whatever their uncertainties, and for all the variations of materials and conditions of manufacture gave consistent values in the range of 70-700 kg/mm². These compare reasonably to the elastic moduli in compression in the high strain regime.

Compression testing provided the clearest and most precise picture of elastic behavior. It was discovered that two plastic strain ranges exist separated by the elastic strain range. Over the initial 3-5% strain range, there was a large irreversible component. Following upon that, there was a strain range of about 2-4% which was purely elastic. Above this, regime strains again were partially irreversible or plastic. This initial mixed strain range is probably artifact.

In all probability, the opposite faces of the compression specimen were not exactly flat or parallel. This initial strain should be regarded as a coining or sizing operation generating parallel faces. In fact, coining is a necessary step in the manufacture of prostheses for dimensional control considerations as well.

Summaries of elastic moduli measured in compression are presented in Figures 4 and 5 for titanium and Vitallium wire. The results are similar in most respects. Wire diameter and sintering temperature in the range of values used do not appear to influence the elastic properties. Accordingly, data points do not make distinctions. Within the range of void contents of 30-60%, there are only slightly distinguishable trends.

The common feature is the transition from a low strain modulus to a high strain modulus. In the range of $0 \approx 0.5\%$ strain, the material can be treated as linear elastic with a modulus of 0.3 to 3.0 kg/mm^2 . These are very low values for a metallic material and signify that for practical purposes it will be remarkably compliant. These also correspond closely to estimates of the elastic behavior of trabecular bone (16) into which prostheses using these materials would be most commonly implanted.

Above this strain range there is a transition to a stiffer behavior with elastic moduli showing clearer dependence on void content and a range of 100-300 kg/mm^2 . This is still nearly two orders of magnitude smaller than the solid metal. The total elastic strain range is very large for a metallic material and, as shown in Figure 6 for molded titanium wire, is clearly dependent on void content. The total elastic strain range for molded Vitallium is smaller and does not exceed 2.5%.

As shown in Figure 7, there is no distinguishable yield point in these materials. Considerable strain hardening develops since the ultimate tensile strength is about three times the stress at the elastic limit. At the ultimate strength, sintered

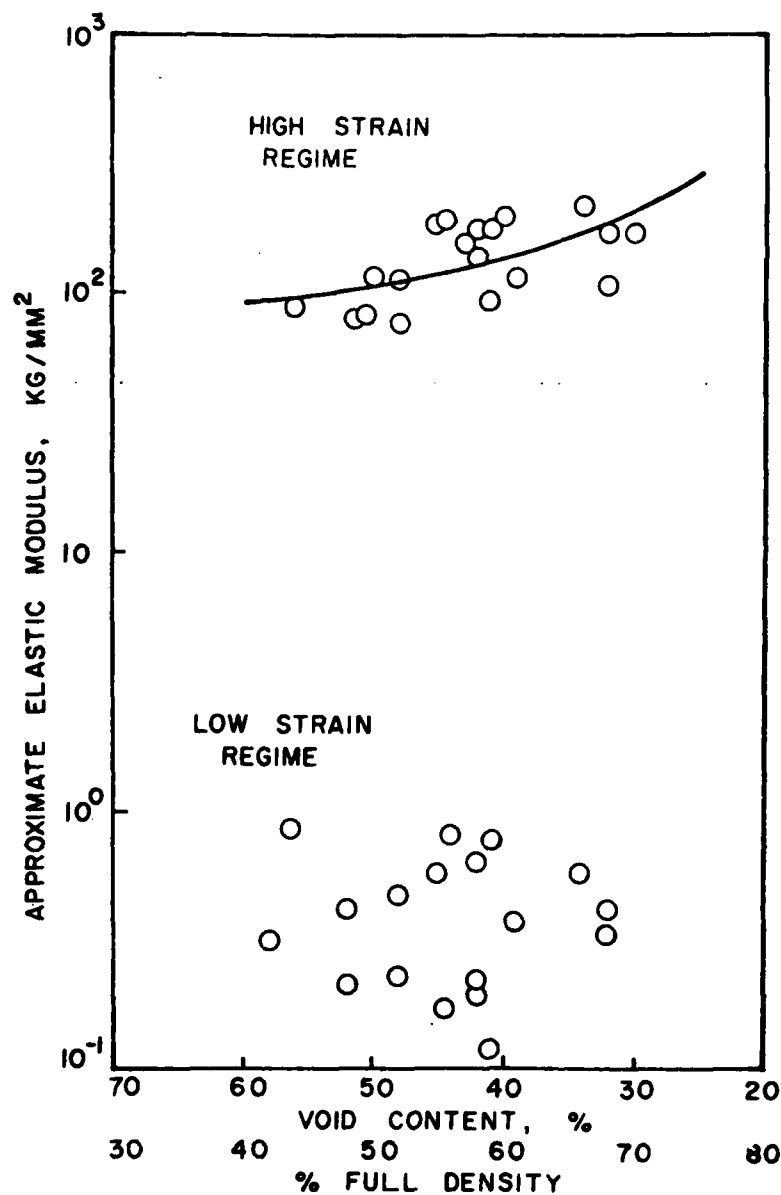


Figure 4

Approximate elastic moduli of molded and sintered titanium wire. ($E=1.2 \times 10^4$ kg/mm² for solid titanium).

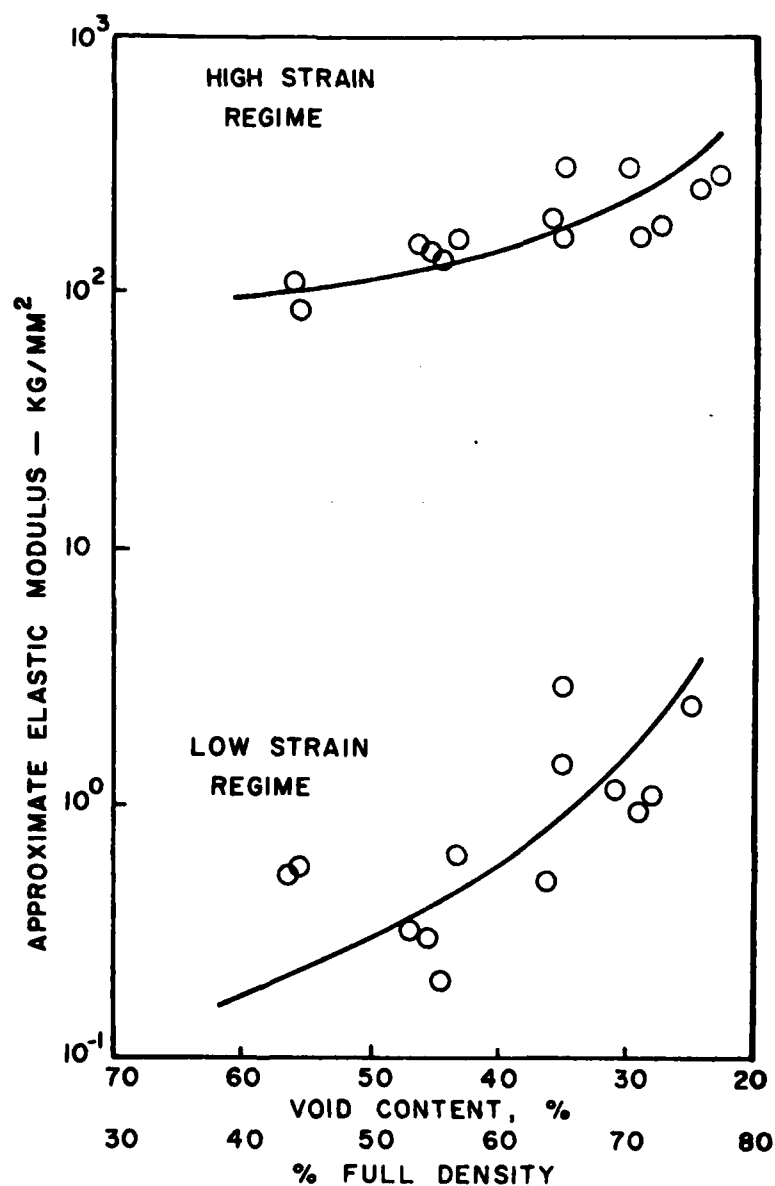


Figure 5

Approximate elastic moduli of molded and sintered Vitalium wire. ($E = 2.3 \times 10^4$ kg/mm² for solid Vitalium).

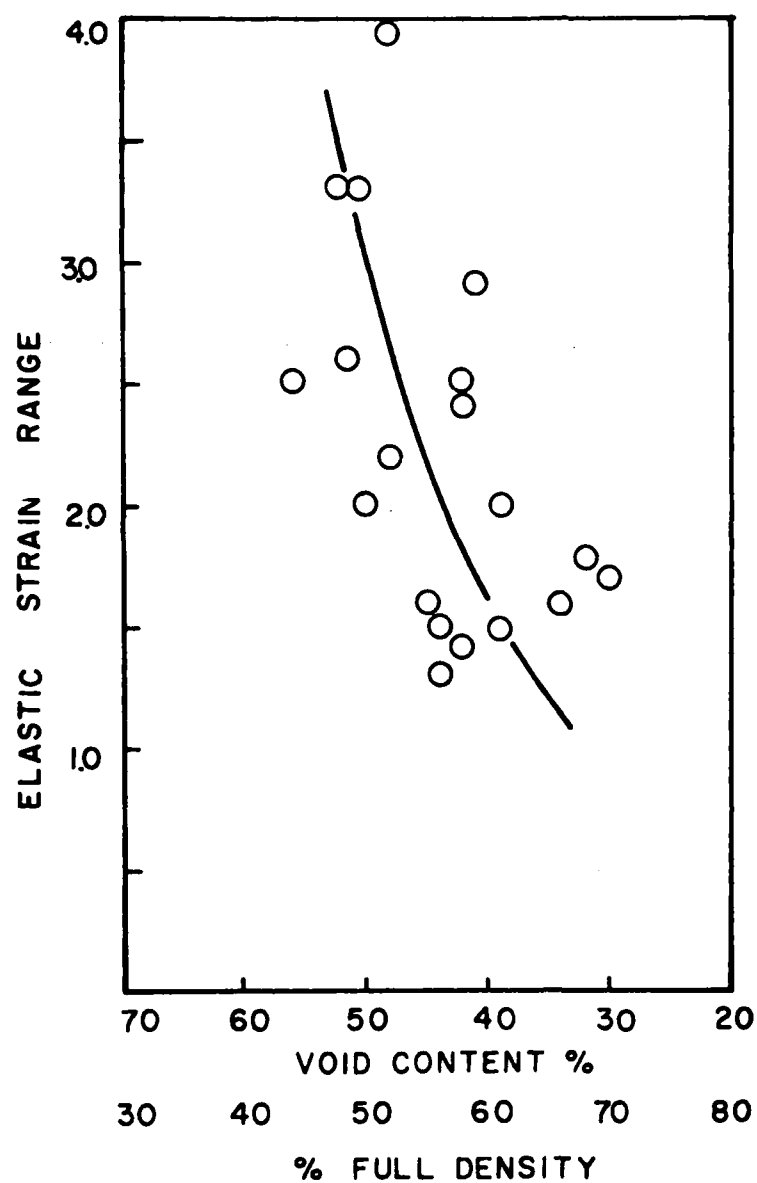


Figure 6

Influence of void content on the total elastic strain range of molded and sintered titanium wire.

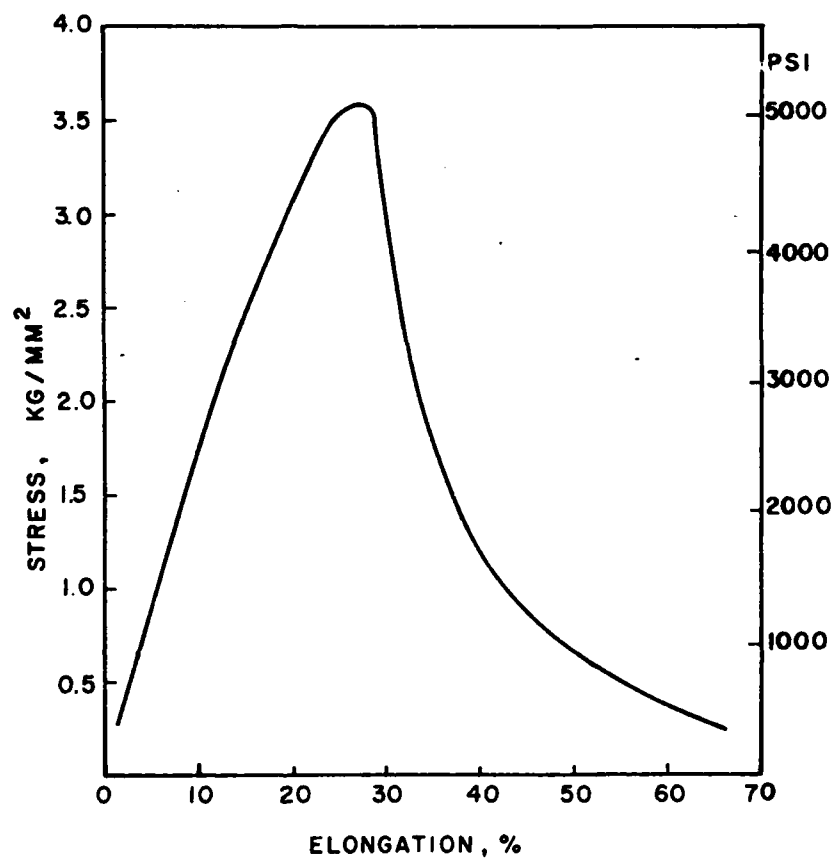


Figure 7 Exemplary tensile stress-strain curve (molded 0.25 mm titanium wire, 42% void, sintered at 1180°C).

bonds or mechanical interlocks begin to rupture as seen by projecting ends of fibers. Rupturing, however, proceeds over a large strain range. There is no fracture but simply a progressive tearing as with a fabric.

The tensile strength is very significantly influenced by void content as seen in Figure 8. Comparison of the strengths of sintered and unsintered materials shows clearly that the source of the strength is much more mechanically interlocked than sintered bonds.

Discussion

Porous composites produced from molded and sintered fibers or wires have unique elastic properties. They are not linear elastic and they exhibit large hysteresis. If we approximate the elastic behavior as two linear processes--one at low strains and one at higher strains--then we find for a 50% void condition two elastic moduli, one at about 0.3 kg/mm^2 and one at about 100 kg/mm^2 . When expressed as percentages of observed modulus to the modulus of a void-free solid, these numbers represent about $10^{-3}\%$ and 0.3% , respectively. In neither case do these compare at all closely with theory and other published experimental work.

Mackenzie (14) developed a theory relating bulk and shear moduli to void fraction for a hypothetical solid populated with spherical pores. Coble and Kingery (15) modified the relations to treat the relationship for Young's modulus. In effect with a void fraction of about 0.5, the relationship predicts that Young's modulus will drop to about 30% of the void-free solid. Experimental data on sintered alumina showed a drop to about 25% of dense alumina which is good agreement.

Drawing on a large number of measurements on sintered iron powder and prior data in the literature, McAdam (16) constructed an empirical relation between Young's modulus and void fraction which predicts a drop to about 10% of the void-free solid value for iron at 50% void. This is, of course, not in very good agreement with

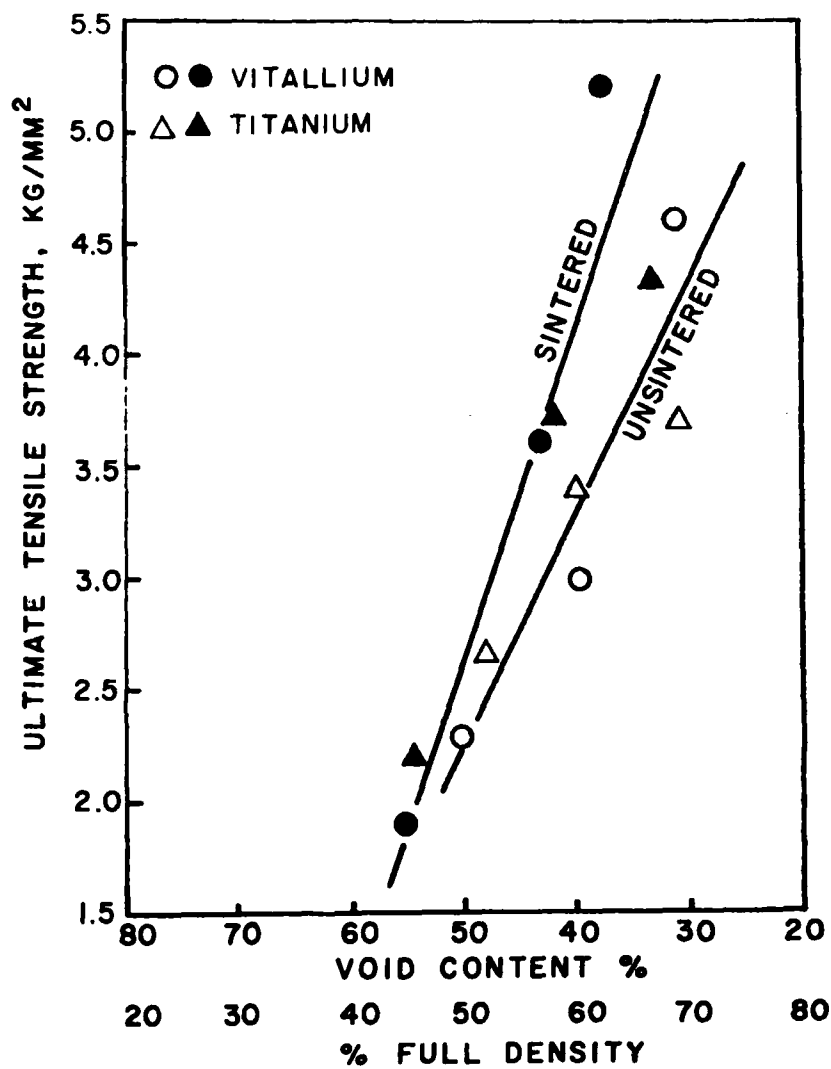


Figure 8

Influence of void content and sintering on the tensile strength of molded wire.

Mackenzie's theory and Coble-Kingery data. Pore shape could be indicated as the distinguishing factor. Mackenzie's theory postulated spherical pores; Coble and Kingery's alumina possessed largely equi-axed pores. But molded and sintered iron has pores which are usually much more lenticular.

Only Bal'shin and Fedtov (17) treat the subject of porous materials produced from fibers. Stainless steel and copper wires of 0.05 mm diameter were cut to lengths of about 7 mm. They were molded to round rectangular bars and sintered. The sintering temperatures were in both cases close to the melting point. Their measurements indicate that the modulus dropped to about 14% of the void-free solid value at 50% void. It is difficult to make a comparison with the present work because essential details of processing, resulting structure and testing procedure are missing.

Clearly the elastic behavior of molded and sintered metal wire or fiber is quite different from sintered powders (both metallic and ceramic). The differences most likely originate from the differences in model. Sintered powders reasonably approximate the Mackenzie model which is a distribution of spherical pores in a solid continuum. On the other hand, molded and sintered fiber can more realistically be characterized as a lattice or three-dimensional grid of metal. From an elastic deformation viewpoint, this model is dealing with the flexure of long slender columns and long multiply supported slender beams. With this kind of model, the very low modulus behavior is reasonable. As deformation strains proceed the long column and long span attributes are eliminated by mutual interaction of deflecting fibers and the assembly behaves more like a solid.

From an applications viewpoint, the very high compliance capabilities are valuable. In certain applications, it is proposed to dispose sleeve-like elements of molded and sintered wire on the surfaces of load-bearing devices such as the stem of a hip joint prostheses. The material can now be expected not only to serve as a

basis for bone invasion and natural growth fixation, but also to distribute load in the transfer from the prosthesis to the surrounding bone tissue. The elimination of significant stress concentrations in the bone host could be an important factor in preventing bone resorption and consequent loosening of the prosthesis.

III. DESIGN OF PROSTHESES FOR SKELETAL SEGMENTS

Most of the experimental surgery used the female baboon as the model. Segmental reconstruction was undertaken on large created defects in the femur, tibia and humerus. In external shape these long bones are very similar to the human equivalent except, of course, the dimensions are all smaller. The distribution of cancellous bone in the interiors was also similar in the baboon to the human. Accordingly, much of what was perfected in the design of the baboon prosthesis could be applied to humans largely by scale-up.

The initial designs of the femur segments and tibial segments were basically the same except for length. They constituted a machined tube of high strength, Ti-6% Al-4% V alloy which was sleeved with porous titanium (unalloyed). Figure 9 shows an assembly of components and the composites. The sleeves are short length and thin walled. The thin wall necessitates the short lengths in the interests of uniform porosity. The sleeves are also dovetailed as a feature to resist rotational motion on the tube. Male dovetails are molded at the segment extremities to be dovetailed into the bone fragments. In the assembly the porous metal sleeving overlaps the tube at both ends so that compression and porous metal deformation can ensure good bone contact all around the circle of interface. A clearer view of the arrangement is shown in Figure 10.

Fixation of the tubular prosthesis design was achieved by a combination of a porous Ti sleeved medullary nail and a bone plate. The bone plate was applied with the use of compression as shown in Figure 11. Because of the length of the medullary nail, it was necessary to incline the screws to get past but the deformability of

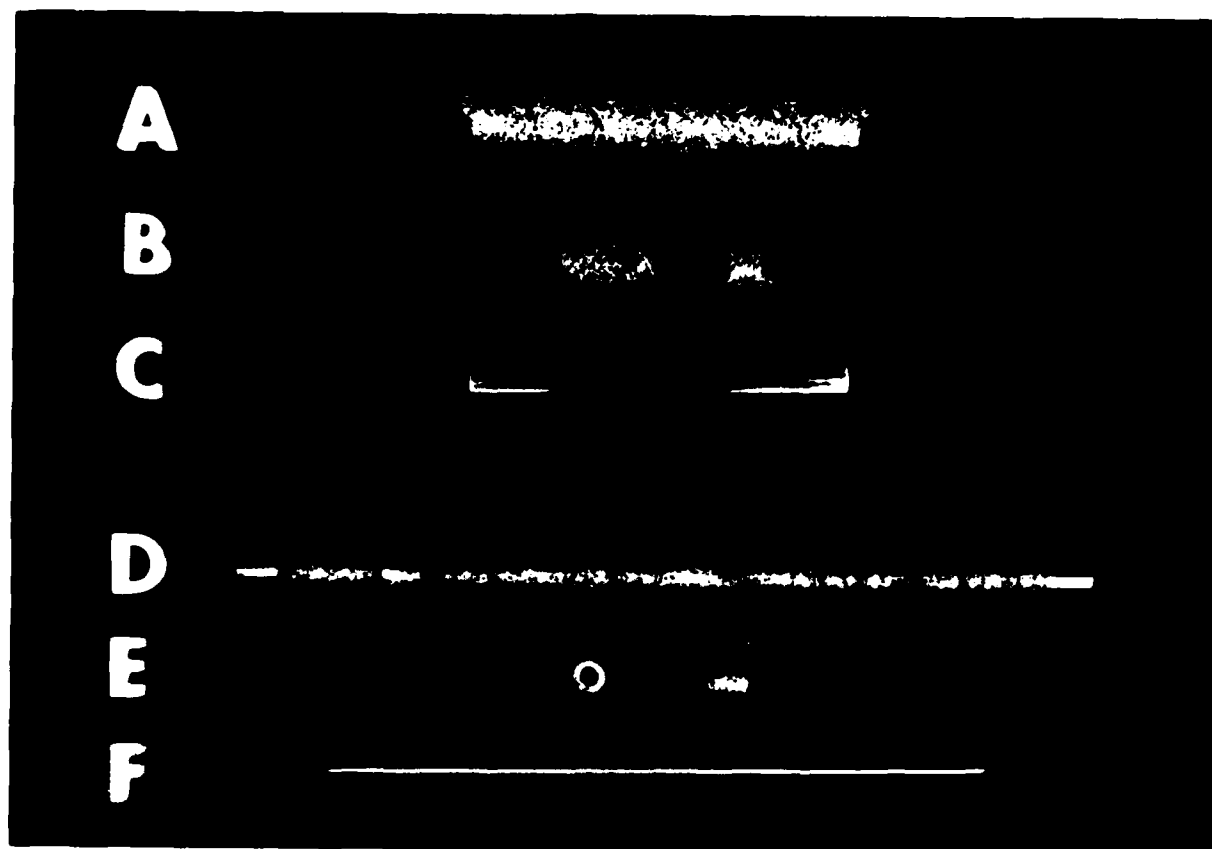


Figure 9

Components and assembly of
a femur or tibial segment
prosthesis.

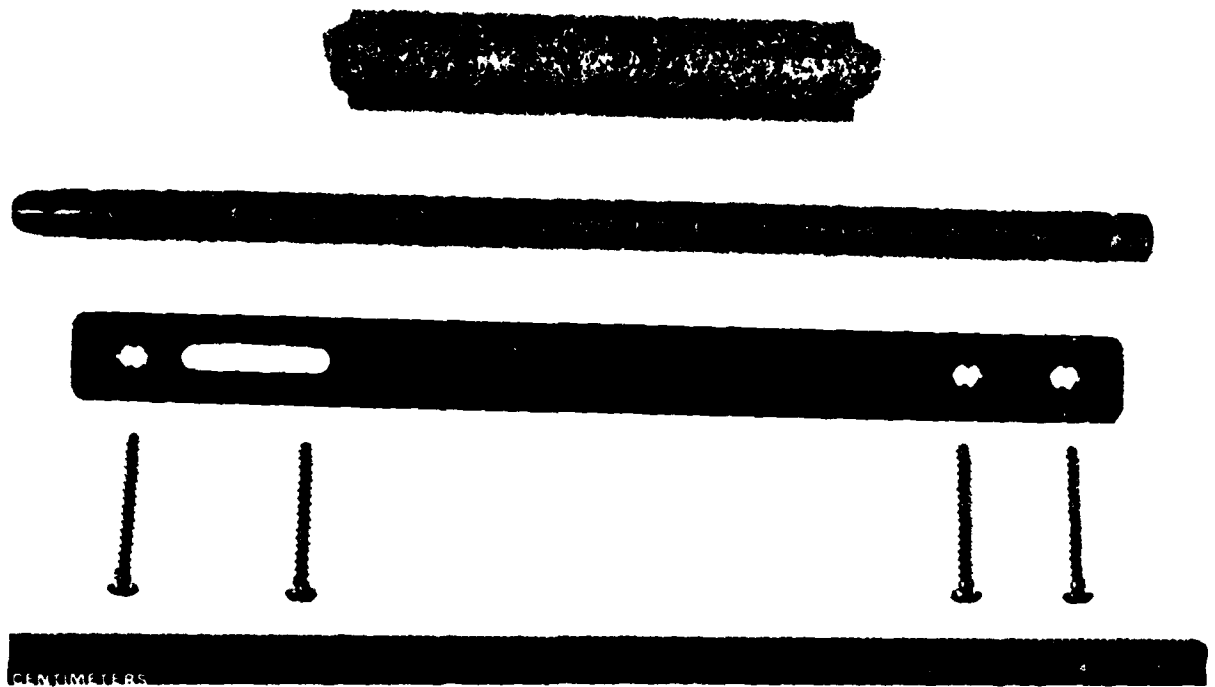


Figure 10

Femur or tibial segment
prosthesis with medullary
nail and plate fixation
components.

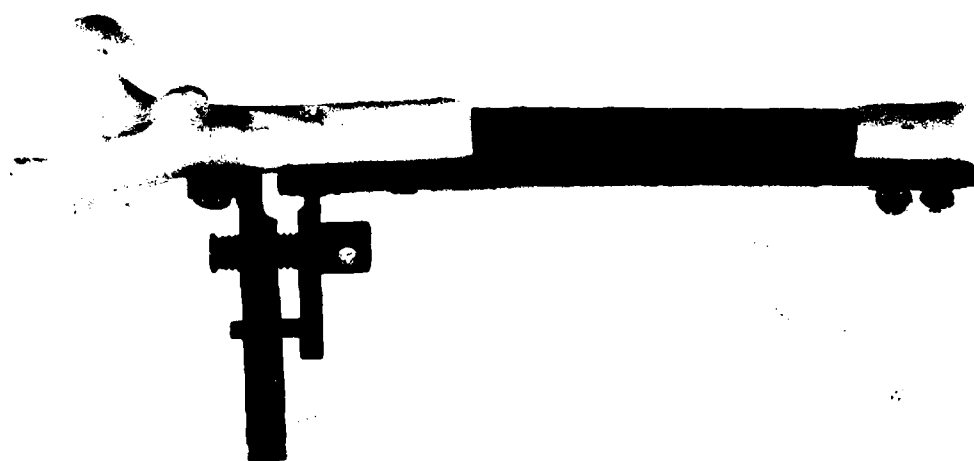


Figure 11 Fiber-metal segmental
replacement in femur
utilizing compression
plating showing AO -
tension device in situ (model).

of the porous surfacing made this a matter of no great difficulty.

In a later design the medullary nail and the segment prosthesis were combined into the single, "rolling pin" unit shown in Figure 12. Plate fixation was retained but the male dovetails at both ends were eliminated as unnecessary in the light of the immobility of the prosthesis with adequate compression.

The humerus segment prosthesis is an adaptation of the femur-tibial design. The major difference which can be seen in Figure 13 is that an attempt has been made to mimic the cross section profile of the natural baboon humerus and thus gain greater area of contact between the bone fragments and the prosthesis at the interfaces.

Some attempts have been made to design, fabricate and test prostheses that combine a segmental reconstruction with a joint replacement. The first of these was a knee joint combined with a femur segment. The tibial component was of stainless steel and was cemented into the site. This was done at a time when wear by polyethylene against titanium was suspect. We now can remove that hazard by proper passivation of the titanium. The polyethylene component was two tires on the femoral extremity. A bone plate attached to the prosthesis and to the femur bone fragment was used for fixation. The external surface of the tibial component was carefully polished to minimize abrasion of the patella. The assembly is shown in Figure 14. It is a rather crude design and would be considerably modified today but the implantation went smoothly and it functioned well for some time.

The combination of a proximal femur reconstruction combined with a hip joint is a recent experiment and has been designed for a dog because it was intended to approach the problem of a cementless acetabulum as well and the site on a female baboon is too small.

The femur component is monolithic incorporating the ball, neck, largely porous-metal-sleeved-segment, a loop for muscle attachment and a porous-metal-sleeved medullary



Figure 12 Rolling pin prosthesis
model.

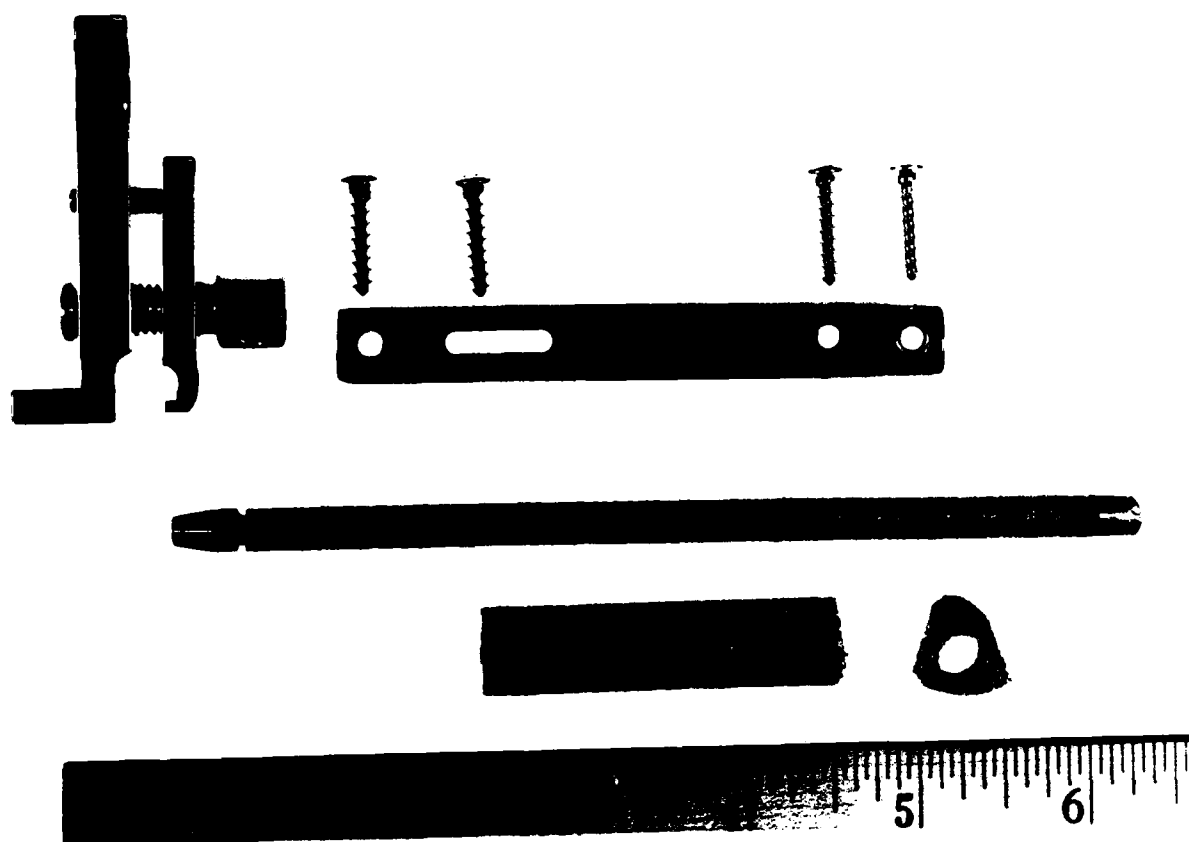


Figure 13

Humerus segment prosthesis
for a baboon with the medullary
nail and the bone plate fixation
systems.

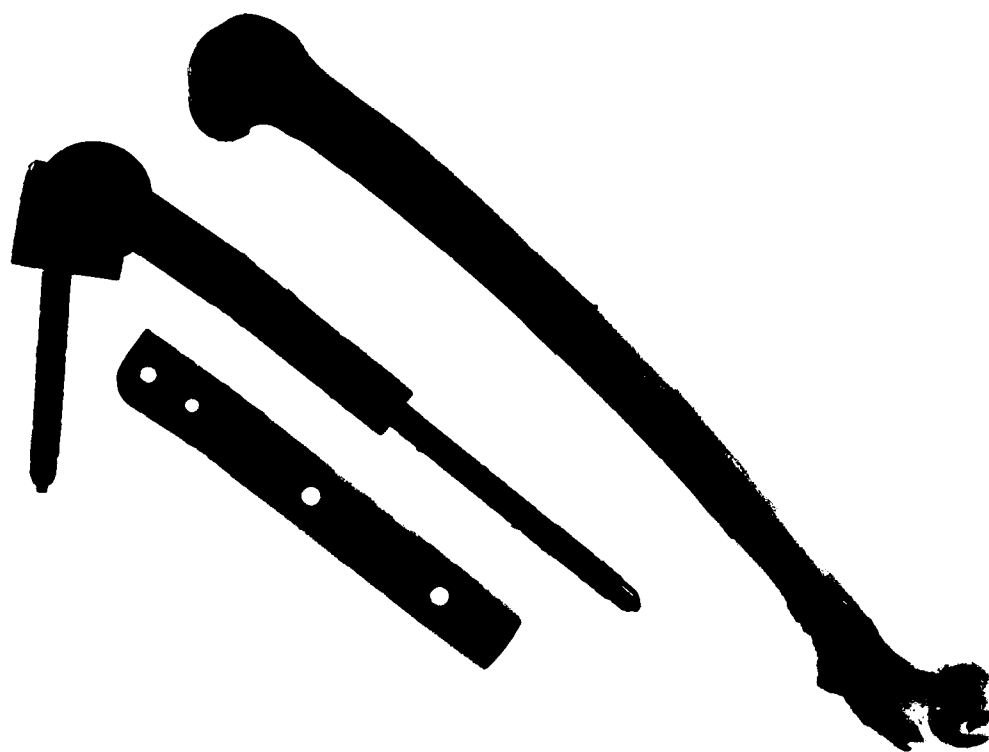


Figure 14

Design of a combination knee joint and distal femur reconstruction for a female baboon using a plate and medullary nail (integral) fixation.

nail. Fixation is to be by bone cement at the distal end of the medullary nail to a length of about 2.5 cm. The design is shown in Figure 15.

The acetabular component represents a major innovation in cementless fixation. We have developed a technique of attachment of porous titanium parts to ultra high molecular weight parts. Basically this is achieved by pressing the assembly so that the hot plastic extrudes into the pores of the metal at the interface but to a depth that leaves the outer porosity available for bony ingrowth. This arrangement for a molded polyethylene acetabulum prosthesis is shown in Figure 16. In this case, the spherical articulating surface was molded at the same time. However, in other applications it would be possible to cover temporarily the porous metal so that the pores do not host particles and to machine the articulating surface in a secondary operation.

The implantation of a cementless acetabulum requires (as do all cementless fixation systems) the preparation of a site to very precise dimensions that represent a zero or slightly negative fit to the prosthesis. This is necessary in the present case not only to ensure bony ingrowth but also to provide some immediate fixation. This approach requires an assembly of special tools for site preparation. These are shown in Figure 17.

IV. SURGICAL PROCEDURE ON BABOON MODEL

In addition to normal standard surgical principles, certain other principles must be adhered to in the insertion of fiber metal prosthetic segments. They include:

1. Preparation of bone ends to insure intimate contact between bone and fiber metal.
2. Good compression of fragments to add stability and to deform the ends of the fiber metal segments for optimum contact.
3. Adequate bone graft (except where protocol calls for no bone graft).

For this experiment, the segments of bone removed were made to correspond in

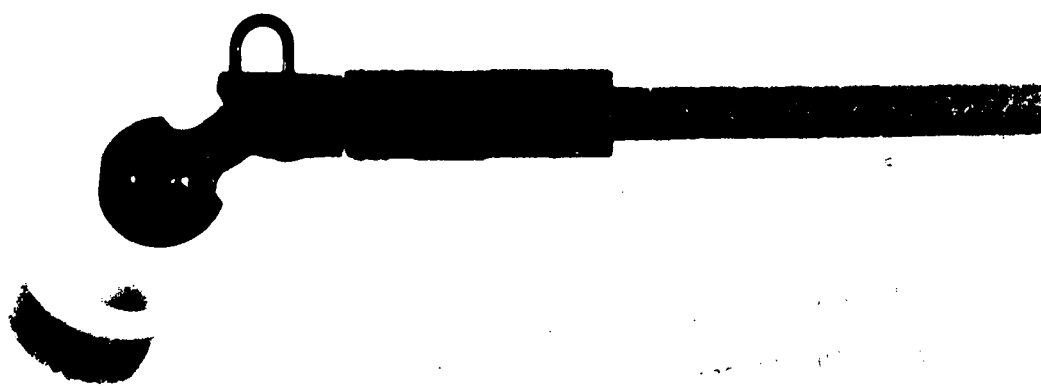


Figure 15

Prosthesis to replace
the upper one-third of
femur and the hip joint
in dogs.

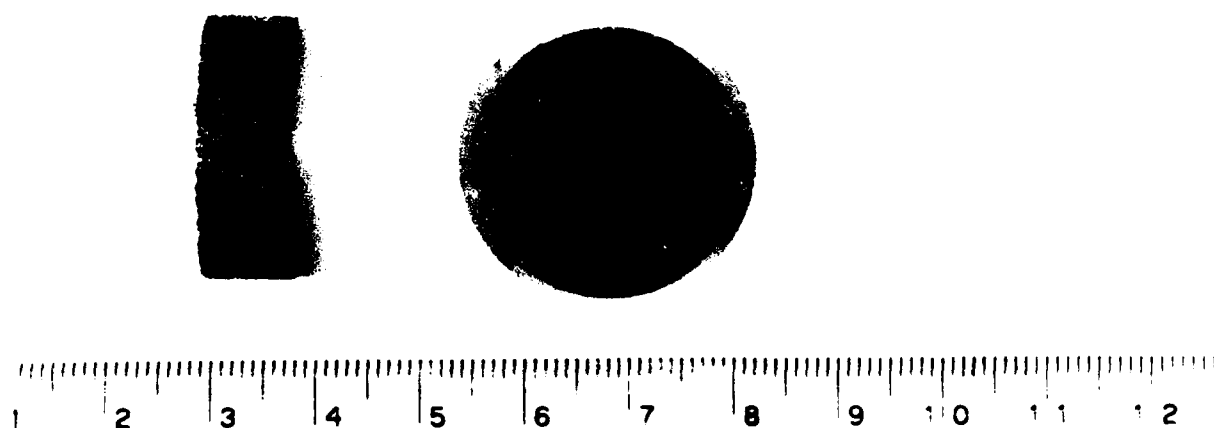


Figure 16

Molded cementless
acetabular prosthesis -
dog model.

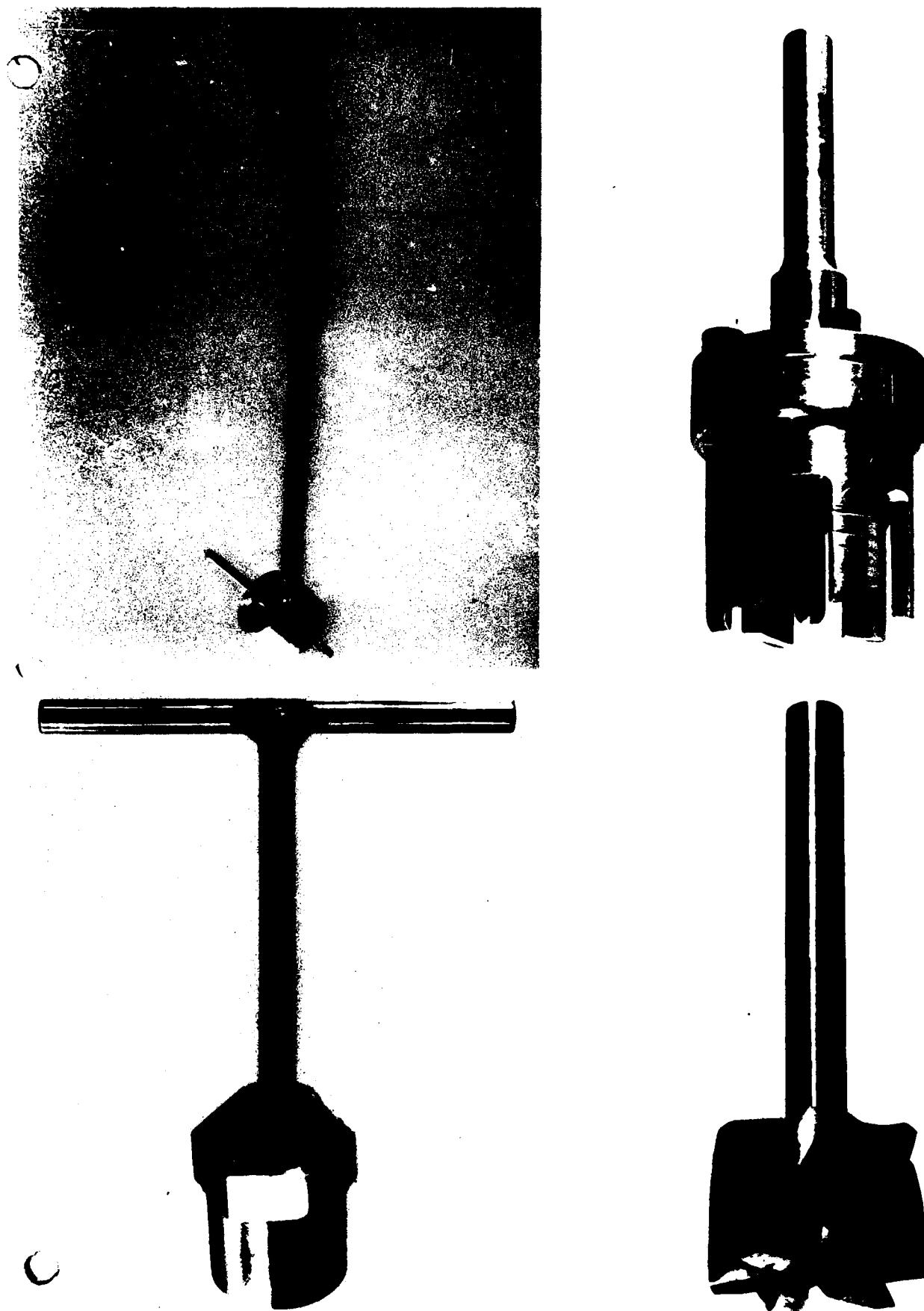


Figure 17

Surgical tool assembly for acetabular prosthesis implantation.

length to the prosthesis. The prosthesis is designed, however, so that its length can easily be tailored to fit a wide range of requirements, and it is anticipated that for human implantation the prosthesis will be made to correspond to the segment of bone removed.

Details of the procedure for segmental replacement of the tibia are herein described in detail and necessary modifications for humeral and femoral replacement are listed briefly. The procedure for replacement of the distal femur and knee is also described in detail. The modifications for the hip/femur segment are summarized.

A. Surgical procedure for segmental replacement of the tibia

The baboon is placed in the supine position and the left lower extremity is prepped from groin to ankle and draped free. An incision is made along the antero-medial subcutaneous border of the tibia extending from the lower border of the patella to just proximal to the ankle. The incision is carried down sharply through subcutaneous tissue to the periosteum and the entire diaphysis of the tibia is extra-periosteally dissected from the surrounding musculature and hemostasis is obtained. A specially designed drill guide is then placed along the medial surface of the mid shaft of the tibia and held in place with Verbrugge clamps. Two 1/4-inch holes corresponding to the length of the prosthetic segment are drilled and the guide removed. Using an oscillating Stryker saw, the tibia is then osteomized in a plane perpendicular to its axis at the levels of the proximal and distal drill holes so that a segment of tibia 2 mm longer than the fiber prosthesis replacement is removed.

Next, the insertion of the patellar ligament is incised longitudinally to expose the surface of the tibial tubercle and a 1/4-inch diameter drill hole is made in the tubercle and the drill is directed obliquely down the medullary canal of the proximal fragment. The distal fragment is also reamed to 1/4-inch diameter to accommodate the intramedullary rod. Trial reduction with the segment is performed, and further

tailoring of the ends of the bone is done with a rasp to insure optimum contact at all points. The fibula is then osteotomized removing a 1-cm segment from the proximal third to prevent distraction of the fragments.

The fiber metal segment is then placed in the appropriate defect and the intramedullary rod (which is equipped with a driver that screws into the tapped proximal end) is directed into the hole in the tibial tubercle and driven down through the segment into the distal fragment to just proximal to the ankle. A specially designed compression plate is placed along the lateral surface of the tibia and attached proximally with two screws that pass on either side of the intramedullary rod and cross both cortices, after tapping the appropriate holes. A standard Mueller compression apparatus is attached distally and tightened until the system is stable and the proximal and distal ends of the fiber metal segment have deformed to give intimate contact with the bone ends. The distal end of the plate is attached and the compression apparatus removed.

Following this, the wound is copiously irrigated with neomycin-polymixin solution. Match stick grafts made from the removed segment are placed along the entire shaft and held in place with cerclage chromic sutures and the wound is closed in layers taking care to cover the subcutaneous portions of the segment with extensor musculature.

No post operative immobilization is utilized, and each animal receives prophylactic antibiotics for five days.

B. Surgical procedure for segmental replacement of the femur

A standard lateral approach to the femur is used and the intramedullary rod is passed through the greater trochanter.

C. Surgical procedure for segmental replacement of the humerus

A standard anterolateral approach to the humerus is used and the intramedullary rod is passed through the greater tuberosity.

D. Surgical procedure for segmental replacement of the femur and knee

The animal is placed on the operating room table in the supine position with a pillow under the left gluteal area to elevate the pelvis. General inhalation anesthesia is used and intravenous fluid replacement is available to correct fluid loss. The left lower limb is prepared and draped in the standard way leaving the thigh and upper third of the leg uncovered.

A lateral exposure of the femur is preferred because it leaves the extensor apparatus of the knee undisturbed. A lateral skin incision down to the fascia lata is performed from a point 15 cm below the great trochanter landmark to 2 cm below the knee joint interarticular line. The incision is slightly curved anteriorly following the curvature of the femur. The fascia is incised and dissected from the underlying muscle. The vastus lateralis is raised from the inner aspect of the lateral flap of the fascia lata. The lateral intermuscular septum was followed by blunt dissection to the lateral tip of the linea aspera. The circumference of the lower third of the femur is exposed incising the periosteum at the linea aspera. Exposure of the middle third of the lateral femoral aspects is obtained dissecting the vastus from the septum and two perforating vessels are ligated and divided. The extent of the exposure is determined by the length of the plate plus the Mueller compression apparatus.

The incision of the fascia is extended down to the interarticular line in line with the skin incision, with special care to preserve the anterior recurrent tibial vessels. The vastus lateralis and knee joint capsule are incised to expose the lateral aspect of the knee joint. The fibular collateral ligament, the anterior and posterior cruciate ligaments are sectioned. The lateral meniscus is removed. The medial aspect of the knee is exposed carefully dissecting under the superficial fascia and a 4-cm longitudinal incision is performed in the medial capsule with a slight posterior inclination to preserve the inferior medial genicular artery and the patellar branches

of the descending articularis genu suprema. The medial collateral ligament is sectioned through this incision and the medial meniscus removed in toto.

The articular capsule, the popliteal, plantaris and two gastrocnemius attachments to the femur are disinserted. The length of femur to be excised is determined by the prosthesis length and the diaphysis sectioned with an oscillating saw. Subsequently, the intramedullary canal is reamed with a 1/4-inch drill and the femoral component of the prosthesis placed to verify if the position is correct.

A 5 mm thick slice of the tibial plateau is cut with an oscillating saw. The plane of the section is perpendicular to the tibial axis. After drilling the tibial shaft, the tibial component of the prosthesis is inserted and a trial reduction is performed to test the orientation of both components. The metal plate is screwed on the prosthesis and the Mueller compression device secured on the femoral shaft. After maximal compression is obtained the plate is secured to the femur with two cortex-to-cortex screws and the compression device removed. Subsequently, the tibial component is cemented with self-curing acrylic cement and the prosthesis reduced in full extension during the setting time to insure proper alignment of the components.

Careful debridement of soft tissue, hemostasis, and removal of cement fragments followed by saline/neomycin irrigation of the wound was the last step before closure. The fascial planes were sutured with interrupted non-absorbable sutures and the skin with interrupted nylon suture. At the end of the procedure the prosthesis appears solidly fixed to the bone and full range of passive flex-extension is present. A long leg cast with the knee in 20° flexion is used to secure initial extension of the knee. The animal tolerates the procedure satisfactorily, the estimated blood loss is 200 cc and 500 cc of 5% dextrose in normal saline are infused during

the procedure. Post operative x-rays show satisfactory placement of the prosthesis. The complete system is in 10^0 of valgus in relation to the femoral axis; this slight deviation was due to the lateral compression plate.

E. Surgical procedure for replacement of the proximal femur and hip joint

The basic surgical procedures utilized are similar to those employed in the replacement of the knee and distal femur. The animal model is an adult dog. The extremity is draped and prepped in a routine manner. The animal is placed in the lateral position. An incision is made for a lateral exposure of the hip joint and proximal femur. The greater trochanter is osteotomized. The capsule of the hip joint is exposed and a complete capsulectomy is performed. The hip joint is easily dislocated. The vastus lateralis is exposed and by extraperiosteal dissection the muscles are lifted from the anterolateral aspect of the femur. The same procedure is carried out with muscular insertions on the posterior and medial sides of the bone. The appropriate segment of bone to be resected is measured and an osteotomy is performed using a driven saw. The intramedullary canal is reamed to receive the intramedullary portion of the prosthesis. The prosthetic device is placed in its trial position to insure adequate contact in the intramedullary canal of the bone and at the prosthesis/bone interface. The acetabulum is then exposed. Special reamers are used to insure a cylindrical cavity of exact dimensions into the bony pelvis. A trial reduction of the prosthetic acetabulum is first performed. A final reduction of the acetabulum is then carried out securing impaction of the fiber metal of the prosthesis into the cavity of the pelvis. Following this, a small amount of acrylic cement is placed in the distal portion of the intramedullary cavity of the femur if the protocol includes partial cementing of the femoral component. If, on the other hand, only cementless fixation is desired, then this portion of the procedure is omitted. The femoral prosthesis is then located in place. If no cement has been used a plate is attached onto the lateral portion of the prosthesis and lateral aspect of the femur

and placed in compression to obtain absolute fixation. The wound is then closed in layers and a routine follow-up as with the other procedures described above is performed.

V. POST-SURGICAL FOLLOW-UP ON THE BABOON MODEL

The animals were housed in cages with inside dimensions of seventy-four by eighty-nine by 117 centimeters. Immediate weight-bearing was not restricted. Five to ten times a day the animals were stimulated to vigorous activity, such as jumping and swinging.

A single dose of thirty milligrams per kilogram of body weight of oxytetracycline was given intravenously one month before death, and a single dose of forty milligrams per kilogram of body weight of chlortetracycline was given one week before death.

Five to fifteen months prior to the last roentgenographic evaluation, the plate and screws were removed from eight of the eleven animals still alive at the time of writing.

After the death of the animal, the entire implanted bone with surrounding soft tissue was removed as well as the following organs: lung, kidney, liver, spleen, pancreas and regional lymph nodes. The replacement segment was first evaluated macroscopically to determine the amount of its surface that was and was not covered by bone. Contact roentgenograms were made of each specimen (anteroposterior, lateral and oblique views) before and after removal of the bone plate. The roentgenograms were rated for bone formation along the surface of the replacement segment, for extent of contact between the replacement segment and bone at the interfaces, and for the presence of any radiolucent areas between the implant and the adjacent bone, using a numerical system. The roentgenographic evaluation was as follows:

Replacement segment: 0 = no or minimum formation of bridging
bone at one or both ends of the replacement segment; 1 = bone

formation at one or both ends but incomplete bridging of the segment; and 2 = uninterrupted bone formation along the segment: complete bridging. Interface (both evaluated separately): 0 = no contact: uninterrupted radiolucent line between the implant and bone ends; 1 = partial contact: areas of intimate contact and radiolucent areas; and 2 = total contact: intimate contact and no radiolucent areas. I_1 = the proximal bone-segment interface, and I_2 = the distal bone-segment interface.

Each specimen including the bone, the replacement segment, and the intramedullary rod was then cut horizontally into five to ten sections. These sections were embedded undecalcified in polymethylmethacrylate, and then thin slices were cut with a diamond saw, horizontally through the intramedullary rods and replacement segments, and vertically through the interfaces between the replacement segment and the host bone. The slices were ground down to a thickness of fifty to 100 micrometers and stained with acid fuchsin. All sections were evaluated histologically and rated by a numerical system. The numerical system was as follows:

Histological evaluation: 0 = no ingrowth of bone; 1 = partial ingrowth of bone: limited ingrowth or ingrowth into less than 50 per cent of the total surface area in the histological section; 2 = complete ingrowth of bone: penetration as far as the solid core in the intramedullary rod over more than 50 per cent of the total surface area on each histological section or ingrowth of bone to a depth of more than five millimeters into the replacement segment over an area of more than 50 per cent of the total surface area in the histological section (the longitudinal section through the bone-prosthesis interface and the transverse section

through the replacement segment).

The intramedullary rod, the interfaces between the replacement segment and the bone, and the replacement segment itself were evaluated separately for bone ingrowth. The combined ingrowth in all areas was also considered.

From each organ removed, two blocks were obtained and several sections of each were studied histologically using hematoxylin and eosin stain.

VI. RESULTS OF THE BABOON MODEL

A. Basic experiments with segment reconstruction

Forty adult female papio-papio baboons, weighing ten to thirteen kilograms, were used. Thirty-six had one implant, three had two implants, and one had three implants, making a total of forty-five segmental replacements. Twenty-three implants were femoral replacements; thirteen, tibial; and nine humeral. At the time of writing, thirty-four implants had been re-examined after removal from animals killed six to seventy-six months after implantation and eleven were in animals still alive forty-eight to seventy-six months after implantation.

Of the thirty-four implants recovered after the death of the animals, seven had been inserted after subperiosteal resection of the bone segment and twenty-seven, after extraperiosteal resection, six of the twenty-seven being controls. Of the seven subperiosteal implants (all femoral), three were studied at six months; two at twelve months; and one each, at thirty-three and sixty months after implantation. Of the twenty-one extraperiosteal experimental implants, eleven were and ten were not supplemented with autologous grafts. The eleven grafted implants were distributed as follows: three in the femur (two studied at six months and one at twelve months); five in the tibia (two studied at six months, two at twelve months, and one at eighteen months); and three in the humerus (two studied at six and one at twelve months). The ten implants not grafted were distributed as follows: three in the femur (one studied at six months and two at twelve months); five in the tibia (one

studied at six months, two at twelve months, and one each at eighteen and twenty-four months); and two in the humerus (one studied at six months and one at twelve months).

The eleven implants (all extraperiosteal) in animals still alive at the time of writing were distributed as follows: four in the femur, three with grafts (sixty months) and one without a graft (seventy-six months); three in the tibia, all with grafts (two for thirty-five months and one for fifty-three months); and four in the humerus, three with grafts (sixty months) and one without a graft (fifty-three months). (Table I).

There were no operative or post operative complications. All animals used their limbs on the first post operative day and within two weeks their behavior was the same as it had been before surgery. When the animals were stimulated to activity, no differences were noted between the limb with the replacement segment and the opposite limb at any time after two weeks.

Roentgenographic Findings

All replacement segments remained roentgenographically intact, but one intramedullary rod in a humerus broke near its distal end. In this instance, there was non union at the distal segment-bone interface and evidence of gross motion of the implant within the distal segment of the humerus. Uninterrupted bone formation along the full length of the replacement segment was seen in thirteen (six of six femora, four of eight tibiae, and three of six humeri) or 65 percent of twenty limbs in which the bone segment had been resected extraperiosteally and bone grafts had been placed around the replacement segment, and in five or 71 percent of the seven femora in which the bone segment was resected subperiosteally. Bone formation along the replacement segment did not occur in any of the four femora, five tibiae, and three humeri in which the bone segments were resected extraperiosteally without simultaneous

TABLE I
SURGICAL TECHNIQUES AND TEST PERIODS

BONE	TYPE OF IMPLANT	MONTHS AFTER IMPLANTATION										NO. OF IMPLANTS
		6	12	18	20	24	33	48	53	60	76	
Femur	Controls (all extraperiosteal with graft)	3	2		1							6
	Subperiosteal (no graft)	3	2				1			1		7
	Extraperiosteal with graft	2	1							3*		6
	Extraperiosteal without graft	1	2								1*	4
Tibia	Extraperiosteal with graft	2	2	1				1*		1*	1*	8
	Extraperiosteal without graft	1	2	1		1						5
Humerus	Extraperiosteal with graft	2	1							3*		6
	Extraperiosteal without graft	1	1						1*			3
TOTAL												45

* Animals still alive at time of writing.

bone-grafting. The numerical ratings derived from roentgenographic and histological evaluations of the replacement segments are given in Tables II and III.

The development of the bone bridge along the replacement segment was time-related. Of the fourteen successfully bridged segments in the extraperiosteally resected and grafted group, two were bridged completely by bone at six months, thirteen at one year, and fourteen at two years. The proximal and distal interfaces between the replacement segment and bone were evaluated separately on the basis of the extent of intimate contact between the implant and bone (no radiolucent line between bone and metal). Total contact - that is, intimate contact at all areas viewed on the roentgenograms - for the most part occurred in animals with bone bridging the segment. In animals with bone grafts, total contact was found in eleven of twelve femoral interfaces (92 percent), in all twelve humeral interfaces (100 percent), and in eleven of sixteen tibial interfaces (69 percent). In the seven limbs with subperiosteally resected bone segments, total contact was found at nine of the fourteen interfaces (64 percent), while in the non-grafted extraperiosteally resected group of twenty-four interfaces, there were three interfaces with total contact (12.5 percent), nine with partial contact (37.5 percent), and twelve with no contact.

In only one of the six control animals was there roentgenographic evidence of uninterrupted bone formation bridging the replacement segment as well as partial bone-implant contact visible at the interfaces. This prosthesis was one that had a solid replacement segment and a solid metal rod. In all six control animals, radiolucent areas of considerable size were visible around all parts of the prosthesis, clearly distinguishing these implants from the others.

In the eight animals from which the plates were removed, subsequent roentgenograms showed no changes and all eight animals continued to be fully active and weight-bearing. Figure 18 illustrates a long term remodelling.

TABLE II

HISTOLOGICAL AND ROENTGENOGRAPHIC EVALUATION OF THE ANIMALS KILLED* (Mean values are given according to the numerical rating system)

BONE SEGMENT REPLACED	TIME WHEN KILLED (Mos.)	NO. OF IMPLANTS	HISTOLOGICAL EVALUATION [†]			ROENTGENOGRAPHIC EVALUATION [‡]				
			SEGMENT	I ₁	I ₂	ROD	SEGMENT	I ₁	I ₂	
Autologous bone graft										
Femur	6	2	1,1	2,1	2,1	2,2	2,2	2,1	2,2	
Tibia		2	1,0	2,0	2,2	1,0	2,1	1,0		
Humerus		2	1,0	2,0	2,2	1,1	2,2	2,2		
Femur	12-18	1	2	2	2	2	2	2	2	
Tibia		3	1,1,0	2,1,0	2,2,1	2,2,1	2,2,1	2,2,1		
Humerus		1	1	2	2	2	2	2		
No bone graft										
Femur	6	1	0	0	0	2	0	0	0	
Tibia		1	0	0	0	0	0	1	1	
Humerus		1	0	0	0	1	0	0	0	
Femur	12-24	2	1,0	0,0	2,0	1,1	1,0	1,0	2,0	
Tibia		4	1,1,0,0	1,0,0,0	1,1,1,0	2,2,2,0	0,0,0,0	1,1,0,0	2,2,1,1	
Humerus		1	0	1	0	1	0	0	0	
Subperiosteal resection										
Femur	6	3	1,1,1	2,0,0	0,0,0	2,2,1	2,2,1	2,1,0	2,0,0	
	12	2	1,1	1,1	2,1	2,2	2,1	2,2	2,2	
	36	1	0	2	0	1	2	2	1	
	60	1	2	2	2	2	2	2	2	

* See Table IV for controls.

† Histological evaluation: 0 = no ingrowth of bone; 1 = partial ingrowth of bone; limited ingrowth or ingrowth into less than 50 per cent of the total surface area on each histological section or ingrowth of bone to a depth of more than five millimeters into the replacement segment over an area of more than 50 per cent of the total surface area in the histological section (the longitudinal section through the bone-prosthesis interface and the transverse section through the replacement segment).

‡ See Table III for this rating system.

TABLE III

ROENTGENOGRAPHIC EVALUATION OF ANIMALS STILL ALIVE*

BONE SEGMENT REPLACED	MONTHS AFTER IMPLANTATION	BONE GRAFT	NO. OF IMPLANTS	ROENTGENOGRAPHIC EVALUATION†		
				SEGMENT	I ₁	I ₂
Femur	60	Yes	3	2,2,2	2,2,2	2,2,2
	76	No	1	0	0	0
Tibia	48	Yes	1	2	2	2
	60	Yes	1	2	2	2
	76	Yes	1	2	2	2
Humerus	53	No	1	0	0	0
	60	Yes	3	2,2,1	2,2,2	2,2,2

* See Table for controls.

† Replacement segments: 0 = no or minimum formation of bridging bone at one or both ends of the replacement segment; 1 = bone formation at one or both ends but incomplete bridging of the segment; and 2 = uninterrupted bone formation along the segment: complete bridging.

Interface (both evaluated separately): 0 = no contact: uninterrupted radiolucent lines between the implant and bone ends; 1 = partial contact: areas of intimate contact and radiolucent areas; and 2 = total contact: intimate contact and no radiolucent areas. I₁ = the proximal bone-segment interface, and I₂ = the distal bone-segment interface.

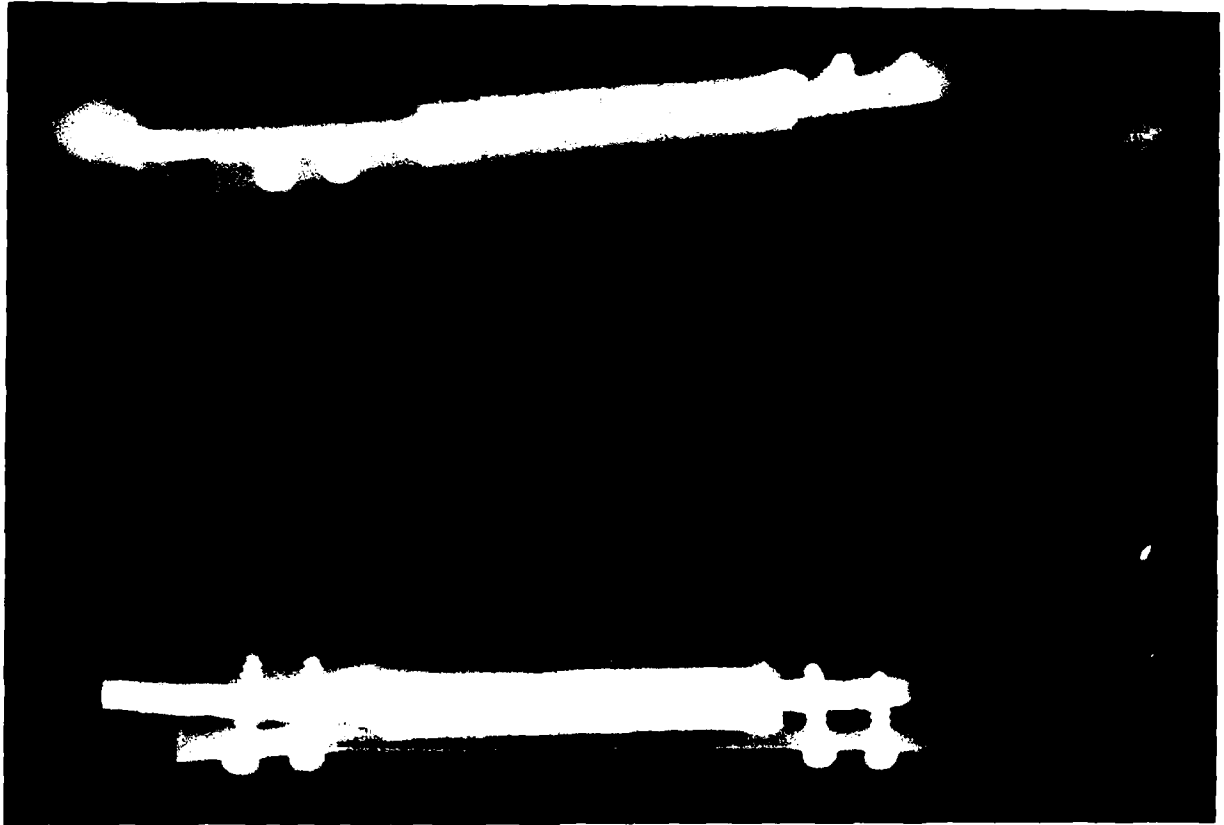


Figure 18

Five year baboon reconstruction.

Autopsy Findings

All plates were intact at autopsy, but one screw was broken in the humerus in which the rod was fractured. In all animals with roentgenographic bridging of the replacement segment by bone, an uninterrupted layer of bone covered the segment, except under the plate which was always separated from the segment by a thin layer of fibrous tissue. All segments in which bone formation had not occurred were covered with a similar fibrous-tissue layer, which was tightly adherent to the fibermetal framework. No signs of infection or gross evidence of tissue intolerance were noticed. In two unstable specimens, both without a bone bridge, small amounts of black-staining material were found in the fibrous tissues between the fiber metal replacement segment and the plate, indicating wear due to motion between the two components in these grossly unstable specimens. Both specimens were femoral replacements for defects in which extraperiosteal bone resection was done without bone-grafting.

Histological Findings

In twenty-six (93 percent) of the twenty-eight experimental prostheses recovered after the death of the animal, there was ingrowth of bone into the sintered intramedullary metal rod. This bone ingrowth was uninterrupted and extended as far in as the solid core in nineteen of these twenty-six implants (69 percent of the twenty-eight rods) and was incomplete in the other seven rods. In the remaining two implants (both inserted after extraperiosteal resection without bone grafts), there was no bone ingrowth and the rod was encased in fibrous tissue. One of these implants was in a femur and the other in a tibia, and neither one was bridged by bone.

The amount of ingrowth of bone into the implants at the interfaces between the replacement segment and the bone was related to the type of surgical procedure performed, to the site of the implants, and to the duration of implantation. In

the eleven animals with bone grafts that were studied histologically, bone ingrowth was found at seventeen of the twenty-two interfaces (77 percent), and of these seventeen interfaces, eleven showed complete and six, incomplete growth. In the seven animals with subperiosteally resected femoral segments, ingrowth was seen at eight of the fourteen interfaces (57 percent), and this ingrowth was complete in five and incomplete in three. In the ten animals with extraperiosteally resected bone segments and no bone grafts, ingrowth was found at six of the twenty interfaces (30 percent) and was complete in only one.

Considering the site of implant, bone ingrowth at the segment-bone interface was more frequent in the three femoral implants (ingrowth present in six and complete in four of the six interfaces) than in the five tibial implants (ingrowth present in seven and complete in four of the ten interfaces) or in the three humeral implants (ingrowth present in four and complete in two of the six interfaces).

The longer the duration of implantation, the greater the bone growth. Thus, in animals with bone grafts, ingrowth was found at eight of twelve interfaces at six months and at nine of ten interfaces at later times of death. In the non-grafted animals, ingrowth was found only in those killed at twelve months or later.

Bone ingrowth into the surface of the replacement segments was irregular, occurring in nine of the eleven replacement segments that were completely bridged by bone and studied histologically. In all but two of these nine segments, the ingrowth was superficial.

Of the six control animals, two were killed at six months, two at 12 months and one at 20 months. Bone ingrowth was complete in the fiber metal intramedullary rods, but in the fiber metal replacement segment there was no ingrowth either at its surface or at its two bone-segment interfaces. There was no bridging on the solid rod controls. (Table IV).

In all specimens studied, the bone in the voids of the fiber metal composite

TABLE IV
EVALUATION OF REPLACEMENT PROSTHESES (FEMUR) IN CONTROLS

TYPE OF PROSTHESIS	TIME TO DEATH OR LAST EVALUATION (Mos.)	NO. OF SEGMENTS	HISTOLOGICAL EVALUATION*			ROENTGENOGRAPHIC EVALUATION†		
			SEGMENT	I ₁	I ₂	ROD	SEGMENT	I ₁ I ₂
Solid segment/ fiber rod	6	1	-	0	0	2	0	0 0
	12	1	-	0	0	1	0	0 0
Fiber segment/ solid rod	6	1	0	0	0	-	1	0 1
	12	1	0	0	0	-	0	0 0
Solid segment/ solid rod	6	1	-	-	-	-	2	1 1
	20	1	-	-	-	-	1	0 1

* See Table II for this rating system.

† See Table III for this rating system.

and immediately surrounding the prosthesis was mature, laminated, and in intimate contact with the metal fibers. See Figure 19.

The fluorescence microscopy studies showed remodelling of the bone within the voids of the fiber metal implants, as well as in the surrounding bone. No abnormal reactions were seen in the tissue surrounding the implants or in the organs removed.

By and large, the roentgenographic and histological appearances were consistent. At five interfaces (one tibial and four femoral), however, the roentgenographic appearance suggested bone ingrowth but none was found histologically. In an effort to understand why in some cases bone ingrowth did not occur, the initial post operative roentgenograms were reviewed to determine how close the contact between the implant and bone was right after implantation. The gap between the prosthesis and bone exceeded one millimeter in 80 percent of the specimens (eight femora, seven tibiae, and five humeri) in which bone ingrowth at an interface did not occur, and in only 20 percent of the specimens (nine femora, one tibia, and three humeri) in which ingrowth did occur.

The histological sections of lung, kidney, liver, spleen, pancreas and regional lymph nodes showed no abnormalities.

B. War Casualty Experiment

This phase of the project was undertaken to examine the feasibility of applying the technique and materials of sintered fiber metal skeletal endoprosthetics to the war casualty patient. For this reason some standards of asepsis and surgical technique were deliberately abandoned in an attempt to simulate battle field conditions.

Three operations were performed over a span of three weeks. The first was designed to simulate a war injury, and entailed the creation of a bone and soft tissue defect under contaminated conditions. Immediate post operative care simulated



Figure 19

Thin cross-section
through center of
reconstruction segment
(five years).

that available on the battlefield, and the remainder of the care and surgery was designed to parallel that available after evacuation to a primary care facility.

Operation #1. General endotracheal anesthesia was administered. The leg was shaved but not prepped, and was draped with sterile sheets in the routine manner with the animals in the supine position. The surgeons were gowned, gloved and masked, but had not scrubbed. The tibia was exposed through a curved anterolateral incision from tibial tubercle to just above the ankle. Although care was taken to preserve vital structures, the midshaft of the tibia was isolated from surrounding muscle (extraperiosteally) with no attempt to avoid soft tissue damage, and without the fastidious hemostatic measures that are usually employed. Next, a 5 cm segment of bone and periosteum was removed with the Stryker saw from the midshaft of the tibia. Unthreaded Kirschner wires were drilled transversely across the proximal and distal segments of tibia. Gown and gloves were removed, and a non-sterile long leg cast incorporating the K-wires with the knee and ankle at 90° was applied. The cast was windowed to expose the wound, which then was intentionally contaminated with a finger. The wound was packed with non-sterile gauze and the animal was placed in an immobilizing chair. Twenty-four hours later, the non-sterile dressing was replaced with a sterile one. On the third post operative day intramuscular clindamycin (25 mg/kg/day in divided doses) was begun. These descriptions are illustrated in Figures 20, 21 and 22.

Operation #2. On the fourth post operative day, the animals were returned to the operating room. The cast was removed, and under general anesthesia, and employing all standard aseptic practices, the wound was debrided carefully down to healthy bleeding tissue as were the skin edges. The field was thoroughly irrigated with 1% neomycin solution (500 cc) and the wound was closed in layers, using chromic catgut internally and nylon for the skin. A sterile long leg 90° - 90° cast was applied incorporating the K-wires, and the animal was placed in a standard cage



Figure 20 **Animal immobilizing chair.**



Figure 21

Casted wound. Post
operative first operation.



Figure 22 Device implanted,
immediately post operative.

without additional immobilization. Clindamycin was continued.

Operation #3. On the seventeenth post operative day the animals were once again taken to the operating room. Through an extension of the original incision, the proximal and distal fragments of the tibia were exposed. After removal of the K-wires, the fibula was osteotomized and the remaining tibial segments were trimmed to receive the implant. The endoprosthesis was then implanted in the standard fashion. Bone obtained from the contralateral iliac crest was used for graft around the implant. Fixation was sound, and the wound was closed in layers and covered with collodion. The animal was returned to her cage with no external fixation, and clindamycin was continued for seven more days.

Results

Three animals have been operated on with the war casualty model. War casualty animal #1 (PA 1813) died 15 months after the first procedure from a pulmonary embolism. War casualty #2 (PA 2421) died after 10 months following removal of the plate. Animal #3 (PA 2199) was sacrificed 12 months after surgery. The x-rays showed good bone ingrowth at both ends of the fiber metal segment and no signs of instability in both animals. Animal #1 had persisting infection, there was a non union at one interface, and an incomplete bone bridge. Animals #2 and #3 had union at both interfaces and a complete bone bridge. Bone ingrowth was confirmed by histological examination.

C. Influence of Pore Size on Bone Invasion

Introduction

Bone ingrowth into the voids of many different porous materials has been shown to occur under non weight bearing and weight bearing conditions. In a previous study segmental replacements of long bone were done successfully in baboons using a fiber titanium implant. The structure of that material can easily be changed by changes in

in fiber diameter and in molding pressures. The change in wire diameter immediately increases the pore size.

While small pores may be advantageous in some materials to enhance the mechanical properties, large pores could conceivably increase the shear strength of the bone-prosthesis interface. In addition, the total surface area of the metal would be smaller in composites of that type with positive biological consequences.

The purpose of this work was to study bone ingrowth into a titanium fiber metal composite with two different pore sizes, to study the consequences of differences in pore size on the bone ingrowth per se, and to study the influence of pore size on the shear strength at the prosthesis-bone interface.

Materials and Methods

Twelve female papio-papio baboons, weighing ten to thirteen kilograms, were used. In all animals a 76 mm segment of both femurs was resected and replaced with a fiber metal segment of a rolling pin design that fitted into the bone defect. The segments were all similar except for the thickness of the titanium fibers. In the prosthesis inserted in the right femur the wire diameter was 0.25 mm. In the prosthesis inserted into the left femur the wire diameter was 0.5 mm. The difference in fiber diameter yielded a difference in the average pore diameter of the composite, which was about 300 microns in the .25 mm diameter fiber composite and about 600 microns in the .5 mm diameter composite. Care was taken to insure a close mechanical fit between the prosthesis and the bone. In addition semitubular plates made of Ti6Al4V were applied in compression and held with four stainless steel screws. Autologous grafts were added on both sides using bone from the resected segment and from the iliac crest. The bone was first crushed and chipped to pieces and then ground to an average particle size of 8 mm.

All surgery was performed under general anesthesia using sterile techniques. Both legs were operated in one session. Antibiotic prophylaxis with clindamycin

was given routinely.

The animals were housed in cages with inside dimension of seventy-four by eighty-nine by 117 centimeters. Immediate weight bearing was not restricted. Five to ten times a day the animals were stimulated to vigorous activity, such as jumping and swinging.

A single dose of 30 mg of oxytetracycline per kilogram of body weight was given intravenously one month before death, and a single dose of 30 mg of alazarin complexon per kilogram of body weight was given one week before sacrifice. Radiographs were taken of each animal monthly.

After death of the animal, the entire implanted bone with surrounding soft tissue was removed.

Preparation for histological study and mechanical testing was performed as described above. Indications are that there are no significant differences between the two pore sizes (3.00 microns and 6.00 microns) evaluated in this experiment. There were no histological differences between the two groups. And no differences in the mechanical tests.

D. Influence of Bone Grafting on Remodelling

Introduction

The transplantation of bone tissue is a common procedure in orthopedic and reconstructive surgery. The success of the transplant is related to its osteoconductive properties, its osteoproliferative properties, and its osteoinductive properties (19,32). The reaction of the bone cells to the grafted bone is also important. Both structural and functional qualities of bone grafts appear to influence their osteoconductive properties. Thus, the larger the surface area in relation to the total graft volume the better (18,19,20,24,25,26,27,28,31,32). The osteoproliferative and osteoinductive properties seem to be related also to structural qualities. Anderson (21) studied the behavior of differently sized

cancellous and cortical bone grafts in the anterior eye chamber of rats. Fragments below 1 mm diameter necrotized. Similar observations have also been made in intra-skeletal situations by Keith (30) and Siffert (31).

In a previous study involving 38 adult baboons, 43 segments of a femur, tibia or humerus were replaced with a sintered titanium fiber composite prosthesis (23,29). When autologous bone was grafted uninterrupted bone formed along the full length of the replacement segment. The bone ingrowth into the fiber metal segment was unpredictable, however, and usually occurred only in some areas. It was postulated that this could be due to the type of bone transplant used. Because of the thin iliac crest of the baboons, cancellous bone is not readily available. It was therefore necessary to use the cortical bone of the removed bone segment which was crushed into large fragments. Smaller size particles might have provided better graft implant contact and additional bone ingrowth into the replacement segment.

The purpose of the present study was to compare bone ingrowth into a fiber metal composite when comminuted bone grafts of two different particle sizes were transplanted to bridge a diaphyseal defect.

Six adult female papio-papio baboons, weighing 10 to 13 kilograms were used. In all animals a 76 mm segment of both femurs was extraperiosteally resected, and replaced with a fiber metal segment of a rolling pin design that fitted into the bone defect. The resection was done with an oscillating saw. The intramedullary canal was irrigated with saline but not prepared surgically, and the prosthesis was snapped into place. Care was taken to ensure a close mechanical fit between the prosthesis and the bone. In addition one semitubular plate made of Ti6Al4V was applied in compression and held with four stainless steel screws. Autologous grafts were added on both sides using bone from the resected segment and from the iliac crest. On the left femur of each animal the bone was chipped into large pieces with a mallet and placed around the implant and over the contact areas between

the prosthetic segment and the ends of the host bone. On the right side the chipped bone was further ground using a regular meat grinder to a particle size with a mean diameter of 6.8 mm (standard deviation 2.3 mm), and placed similarly.

All surgery was performed under general anesthesia using sterile techniques. Both legs were operated in one session. Antibiotic prophylaxis with clindamycin was given routinely.

The animals were housed in cages with inside dimensions of 74 x 89 x 117 cm. Immediate weight bearing was not restricted. Five to ten times a day the animals were stimulated to vigorous activity, such as jumping and swinging.

A single dose of 30 mg of oxytetracycline per kilogram of body weight was given intravenously one month before death, and a single dose of 30 mg of chlortetracycline per kilogram of body weight was given one week before sacrifice. Two animals were sacrificed at one month, two at three months and two at six months. Radiographs were taken of each animal monthly. After death of the animal, the entire implanted bone with surrounding soft tissue was removed. The replacement segments were first evaluated macroscopically. Contact roentgenograms were then made of each specimen (anteroposterior, lateral, oblique views) before and after removal of the bone plate. The roentgenograms were rated for bone formation along the surface of the replacement segment and bone at the interfaces, and for the presence of any radiolucent areas between the implant and the adjacent bone. Each specimen was then cut horizontally into ten sections. These sections were embedded undecalcified in polymethylmethacrylate, and then slices were cut with a diamond saw. These cuts were made perpendicular to the long axis of the femur in the areas of the intramedullary rods and the replacement segment, and parallel to the long axis across the interfaces where the replacement segment was in contact with the ends of the host bone. The slices were ground down to a thickness of 50 - 200 micrometers and stained with acid fuchsin. All sections were evaluated histologically for bone ingrowth. Separate

evaluations were made of the area of the intramedullary rod, the interfaces between the replacement segment and the ends of the host bone, and the area of the replacement segment itself.

Results

There were no operative or post operative complications. All animals used their limbs on the first post operative day and within two weeks their behavior was the same as it had been before surgery.

All prostheses, plates and screws remained roentgenographically intact. A bone bridge had not developed along the replacement segment in any of the four limbs at one month. At three and six months uninterrupted bone formation was seen in all limbs. There were no obvious roentgenographic differences between the limbs in which ground bone was transplanted and those in which chips were used.

All plates were intact at autopsy. In the animals sacrificed one month post operatively callus formation was evident along the full length of the replacement segment. In the animals sacrificed at three and six months uninterrupted bone was found covering the segment, except under the plate where a thin layer of fibrous tissue was always present. No abnormal tissue reactions were noted. There was no major evidence of bone resorption in the surrounding intact cortical bone.

Bone ingrowth into the surface of the rods, interfaces and replacement segments occurred at only a few places in the animals sacrificed at one and three months. No difference was found between the animals with ground, and those with large fragment transplants. At six months on the other hand, bone ingrowth was found in all histological sections. A marked difference was observed in the amount of ingrowth between specimens with the two different grafts. In the ground graft specimens ingrowth occurred over the total surface of the segment, and bone penetrated deep into the fiber composite. With the large fragment graft bone ingrowth was irregular occurring only in some areas, and it was always superficial. Fluorescence microscopy showed remodelling of the bone between the fibers where bone ingrowth occurred.

Discussion

The study shows that diaphyseal defects can be successfully bridged by fragmented autologous bone grafts of different particle sizes. Ingrowth of bone was found only in a few sections at one and three months. At six months ingrowth was found in all sections. The ground bone with a smaller particle size was found to be superior with respect to bone ingrowth into the replacement segments. A more even ingrowth into the fiber metal occurred over a larger surface area with the ground bone than with the chipped bone transplants. This can probably be explained by the fact that intimate contact between ground bone graft and fiber metal was obtained over larger surface areas. Anderson *et al.* (22) found that a heterogeneous bone paste with particle size varying from .3 to .7 mm was as rapidly vascularized as autogenous cancellous bone, while in heterogeneous cortical bone particles of 2.8 x 1 mm penetration of blood vessels was limited to 1 mm on the surface. The improved vascular penetration of the graft when it is in form of a paste with a large surface area and an open texture may have been favorable but cannot be confirmed in the present experiment.

The previously mentioned studies by Keith (30), Siffert (31) and Anderson (21) indicate that the critical size of the fragments is 1 mm in diameter. The particle size in this experiment was considerably greater and apparently did not influence the osteoproliferative and osteoinductive potentials of the graft.

The advantages of the ground bone chips over larger cortical pieces of bone is obvious in the handling and spreading of the graft over the surface area of a prosthesis of the type used in this experiment. The lesser bulk of the graft makes this type of grafting particularly useful in areas where the soft tissue covering the bone is thin.

Summary

A study was made of bone ingrowth into fiber metal composite prostheses used to

replace large segments of the femur in baboons. Bone grafts of two different types were used to cover the segment: chips of bone with large particle size and ground bone with a lesser particle size. The prosthetic segment was bridged by bone at three and six months in all cases irrespective of the structure of the transplant. In animals sacrificed at six months bone ingrowth occurred, with a marked difference between specimens with the two different grafts. In the ground bone specimens ingrowth occurred over the total surface area, and bone penetrated deep into the composite. With the chip grafts ingrowth was more irregular occurring only in some areas and it was always superficial. The difference is believed to be due to the improved contact between the fiber metal surface and the transplant. The lesser bulk of the ground transplant is advantageous when the soft tissue cover of the bone is thin.

E. Comparison of Fixation Through Bone Ingrowth With and Without Methacrylate
Introduction

A titanium-fiber metal implant has been used to replace successfully massive segments of long bones in humans and baboons (23,34). Autologous bone transplants were added and a bone bridge developed. Based on the animal experience it was concluded that immediate stable fixation of the implant was important to allow bone ingrowth into the pores of the composite. Such stability could easily be obtained in the animals by the use of bone plates for internal fixation. In the human application, however, the bone plate method is not always possible particularly when the location of the lesion is close to a joint. In that case immediate intramedullary fixation would be enhanced by the use of methylmethacrylate.

The obvious disadvantage of the acrylic in this context is that it prevents bone ingrowth. The long-term fixation of the implant might therefore be less satisfactory, particularly as endosteal bone had proved to be most consistent and reliable source of bone ingrowth (23).

The purpose of the present study was to investigate the occurrence of bone ingrowth into the fiber metal composite of a replacement segment when acrylic cement was used for intramedullary fixation.

Materials and Methods

Four adult female papio-papio baboons, weighing ten to thirteen kilograms, were used. In all animals a 76 mm segment of both femurs were resected extra-periosteally, and replaced with a prosthetic device of a rolling pin design that fitted into the bone defect. The devices were made from solid Ti6Al4V alloy, and incorporated a central segment into which titanium fiber sleeves were sintered. The proximal and distal extensions for intramedullary insertion were either solid or covered with titanium fiber sleeves. The resection was performed with an oscillating saw. The intramedullary canals were not prepared surgically, and the prostheses snapped in place. On the left femur of each animal the device with solid intramedullary pins was used and was cemented in place using sufficient acrylic (Simplex) to fill the intramedullary canal, but making an effort to prevent methylmethacrylate from interposing between the prosthetic segment and the ends of the resected bone (that contact area will be referred to as the interface through this paper). The cement was hand packed into the intramedullary canal after irrigation of the canal with saline. On the right femur the intramedullary rod coated with titanium fiber metal was used and a close mechanical fit was obtained, without the use of bone cement. On both sides of Ti6Al4V semitubular plates were applied in compression and held with four stainless steel screws. Autologous grafts were added on both sides using bone chips from the resected segment and from the iliac crest. Care was taken to completely surround the segment with bone grafts, and to place bone over all contact areas between the prosthetic segment and the ends of the host bone.

All surgery was performed under general anesthesia using sterile technique.

Both legs were operated in one session. Antibiotic prophylaxis with clindamycin was given routinely.

The animals were housed in cages with inside dimensions of 74 x 89 x 117 centimeters. Immediate weight-bearing was not restricted. Five to ten times a day the animals were stimulated to vigorous activity, such as jumping and swinging.

A single dose of 30 milligrams of chlortetracycline per kilogram of body weight was given intravenously one month before death, and a single dose of 30 milligrams of oxytetracycline per kilogram of body weight was given one week before sacrifice. Two animals were sacrificed at three months and two at six months. Radiographs were taken monthly in all animals.

After death of the animal, the entire implanted bone with surrounding soft tissue was removed. The replacement segment was first evaluated macroscopically to determine the amount of its surface that was and was not covered by bone. Contact roentgenograms were made of each specimen (anteroposterior, lateral and oblique views) before and after removal of the bone plate. The roentgenograms were rated for bone formation along the surface of the replacement segment, for extent of contact between the replacement segment and the ends of the cut femur at the interfaces, and for the presence of any radiolucent areas between the implant and the adjacent bone. Each specimen was then cut in half, and the distal half was further cut into four sections. These sections were embedded undecalcified in methylmethacrylate, and then thin slices were cut with a diamond saw. These cuts were made perpendicular to the long axis of the femur in the areas of the intramedullary rod and the replacement segment, and parallel to the long axis across the interfaces where the replacement segment was in contact with the ends of the host bone. The slices were ground to a thickness of 50 to 100 micrometers and stained with acid fuchsin. All sections were

evaluated histologically for bone ingrowth. Separate evaluations were made on the area of the intramedullary rod, the interfaces between the replacement segment and the ends of the host bone, and the area of the replacement segment itself.

The proximal half of the femur was stripped of bone around the interface. The proximal end of the specimen was then embedded in epoxy and fixed into an aluminum cup. In the distal end a drill hole was made through the prosthesis. A cable was then run through the drill hole in the prosthesis and another cable through a similar drill hole in the aluminum cup. The specimens were mounted in a Hounsfield tensometer and a pullout test performed at a speed of 4mm per minute.

Result

There were no operative or post operative complications. All animals used their limbs on the first post operative day and within two weeks their behavior was the same as it had been before surgery.

All prostheses, plates and screws remained roentgenographically intact. Uninterrupted bone formation along the full length of the replacement segment was seen in all limbs at three months. The replacement segment and the host bone were in close contact at the resection areas in all limbs.

All plates were intact at autopsy. An uninterrupted layer of bone covered all segments, except under the plate where a thin layer of fibrous tissue was always found. No abnormal tissue reactions were noted.

Bone ingrowth occurred into the fiber composite of the non-cemented intramedullary rods. At three months the ingrowth was irregular; in some areas bone penetrated up to the solid core of the rod, in some it was more superficial. At six months bone ingrowth was complete.

At the interface between the replacement segments and the ends of the

host bone ingrowth occurred on the cemented and non-cemented side in one three month animal, but on neither side in the other. At six months ingrowth was found at all eight interfaces in both animals.

Bone ingrowth into the surface area of the replacement segment was irregular and superficial in all segments, with more bone growing into the segment at six than at three months.

Fluorescence microscopy showed remodelling of the bone between the fibers as well as in the surrounding bone. No differences were found between cemented and non-cemented specimens.

The ultimate tensile strength (at which point the prosthesis separated from the bone) was found to be greater for the specimens where bone ingrowth into the rod occurred than for the cemented specimens (Table V). Failure in the cemented specimens occurred between the prosthesis and the methylmethacrylate, not between the acrylic and bone. The increase in strength of the bond which was observed in the cemented specimens from three to six months was probably due to the bone ingrowth which occurred into the fiber metal composite at the contact area between the prosthetic segment and the ends of the resected host bone (the interface). In animals with porous intramedullary rods an increase in tensile strength was found at six compared to three months.

Discussion

Uninterrupted bone formation along the full length of the replacement segment was achieved in all limbs. Based on our previous experience, this would indicate good stability of the implant (23). It is uncertain to what degree that stability was provided by the intramedullary fixation and to what degree it was provided by the plate. In any event the system was stable enough to allow bone formation whether or not bone cement was used.

Bone ingrowth into the pores of the fiber metal composite of the intramedullary

Table y The ultimate tensile strength at the eight interfaces.

<u>Animal #</u>	<u>Implantation Period (months)</u>	<u>Fixation</u>			
		<u>Acrylic</u>		<u>Bone Invasion</u>	
		N	$\text{N/m}^2 \times 10^3$	N	$\text{N/m}^2 \times 10^3$
1	3	45	62	3512	4954
2	3	130	186	1334	1884
3	6	1600	2256	4580	6458
4	6	980	1380	5780	8156

rod provided an excellent fixation of the implant as found in the mechanical tests. The shear strength of the bone-fiber metal bond was as good as that reported for other porous materials in the intramedullary situation (35,36). The strength of the cement-bone interface was not adequately tested in these experiments since failure of the system occurred between the rod and the cement. It would seem possible to enhance fixation by designing the stem to interlock in a different manner with acrylic.

In the long term perspective an integration of the prosthesis with the host bone would completely prevent loosening. A total integration can only be achieved when all areas are coated by a porous material and when bone cement is not interposed. The use of bone cement does not preclude an inclusion of the prosthesis within the bone, however. Bone ingrowth occurred into the fiber metal at the interface between the prosthetic segment and the resected bone, providing substantial fixation after six months, and the segment was completely covered with bone. Thus, in time the prosthesis would be completely incorporated, and partly integrated with the host bone. The results of this study indicate that the combinations of acrylic cement to provide immediate fixation and fiber metal to allow bone ingrowth can be an acceptable compromise in internal prosthetic applications.

Summary

A titanium fiber metal implant was used to replace large segments of both femurs in four baboons. Immediate fixation was obtained by bone plates and intramedullary rods. On the left side the rods were coated by fiber metal permitting fixation through bone ingrowth. On the right side the rods were solid and fixation achieved with methylmethacrylate. Two animals were sacrificed at three months, and two after six. The results were evaluated histologically and pull-out tests were done to determine the strength of the fixation.

Complete bone bridging of the replacement segment occurred in all limbs. In the fiber-metal coated rods bone ingrowth was always found, more so after six than after three months. The strength of the bond increased from three to six months in both groups of animals. It is concluded that in the specimens with fiber metal coated intramedullary rods this increase in bond strength was due to an increase in bone ingrowth mainly into the rod, in the cemented specimens to ingrowth of bone into the fiber metal composite of the prosthetic segment at the contact area between the segment and the ends of the host bone, where the femur was resected.

VII. DESIGN OF HUMAN PROSTHESES AND EARLY RESULTS IN PATIENTS

Introduction

Segmental defects in long bones caused by disease or trauma can result in shortening, deformity and severe disability. When large segments are lost, autologous transplantation alone is not suitable as a method of reconstruction and the surgeon may have to use a prosthetic device or revert to amputation. Homologous transplantation from cadaveric bone is another alternative, but at the present time the procedure is still experimental.

We suggest that replacements of major segments of long bones can be successfully carried out using a titanium fiber prosthesis supplemented with autologous bone grafts. This concept was derived from a series of long-term animal experiments in which major segmental resections were reconstructed by this method. Union between the implant and bone was obtained and the fiber metal segment was covered by a layer of uninterrupted living bone extending from the proximal to the distal part of the resected bone.

In this report the results observed in a series of twelve patients who underwent segmental replacement for severe bone loss secondary to trauma or resection for tumors were described.

Methods

The technical details and mechanical properties of the porous titanium fiber composite used have been described in detail previously. The replacement prostheses consisted of solid Ti 6% Al 4% V rods on to which titanium fiber sleeves were sintered. They were made after x-ray measurements to fit the individual patient. A rolling pin design was adopted with a central replacement segment and distal and proximal projections designed to be inserted into the intramedullary canal or into matching drill holes in cancellous bone. Early fixation was obtained by means of Ti 6% Al 4% V plates attached to the bone by stainless steel or titanium screws using compression techniques. In one of the patients methylmethacrylate was used to obtain additional fixation of the intramedullary pins. Autologous iliac bone grafts were used routinely. In three of these patients the prosthetic device was used to arthodese the knee joint.

Case Histories

Case #1. A 62 year old female fractured her right tibia on September 21, 1975 after sustaining minor trauma. X-rays revealed a pathological fracture. Further investigation disclosed a diagnosis of metastatic endometrial carcinoma. No other metastasis were discovered. In October, 1975 a 9.5 cm segment was removed from the right tibia and replaced by a fiber titanium implant. As the distal resection line of the segment was near the ankle joint, the prosthesis was anchored with bone cement in the intramedullary canal to provide additional initial fixation. Plate and screws were applied and iliac bone grafting was completed. Histology showed the lesion to be adenocarcinoma with squamous metaplasia. The patient was treated post operatively with pelvic radiation (5300 rads) for her primary endometrial carcinoma. She was discharged on November 25, with the leg immobilized in a PTB plaster cast. On December 3, the plaster cast was removed and a cast brace was utilized with partial weight bearing. The brace was removed on May 5,

at which time the patient was full weight bearing and walking without supports and without a limp. There was no pain and the range of motion of the ankle joint was only slightly impaired. X-rays showed complete bridging of the segment without radiolucent areas. On July 8, 1976 the patient died suddenly due to myocardial infarction. Post mortem examination of the tibia showed complete bridging of the replacement segment by bone and x-rays revealed close contact between implant and bone. The thickness of the covering bone varied from 1 to 5 mm. Figure 23 illustrates this case.

Histologically, new bone formation was observed around the prosthesis. Some bone trabeculae were also seen between the fibers of the implant, particularly at the prosthesis-bone interfaces proximally and distally.

Case #2. A 28 year old previously healthy male who in October, 1975 experienced sharp pain in the right medial aspect of his tibia after physical exercise. The pain subsequently disappeared but reappeared on January 20, when an x-ray showed a lytic lesion in the left tibial condyle. A biopsy revealed a diagnosis of fibrosarcoma. Surgery with excision of a 10 cm long segment of the tibia including the tumor was performed on January 29. The defect was temporarily filled with acrylic cement. The leg was placed in a plaster cast and the patient was then referred to us for possible reconstruction. On March 31, 1976, a 12.5 cm long fiber metal titanium prosthesis was used to replace the resected segment and arthrodesis the knee joint. Because of difficulties to close the skin, bone grafting could only be done medially, laterally and posteriorly. A cylinder cast was applied and the patient was discharged on April 13. The patient was readmitted on August 28 for iliac bone grafting anteriorly. During surgery solid bone formation and bridging from the femur to the tibia was observed over the posterior, lateral and medial aspect of the fiber implant. Histology of bone removed at the time of surgery disclosed viable bone overlying the prosthetic device. The

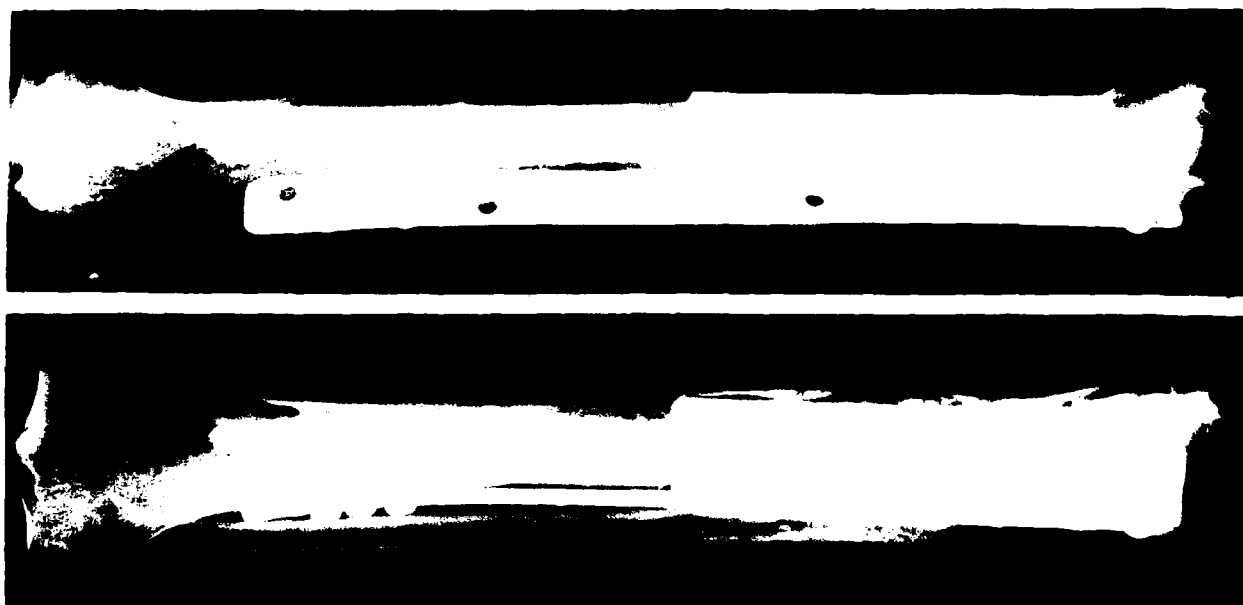


Figure 23

Post mortem
radiographs of
isolated tibia -
Case #1.

patient is at present ambulating with full weight bearing. Figure 24 illustrates the case 22 months post operative.

Case #3. A 30 year old male farmer complained of pain over the left knee after a fall in 1975. X-rays obtained in February 1976 showed a large lytic lesion involving the distal end of the left femur. A trocar biopsy was performed and a diagnosis of giant cell tumor was made. On April 20 the distal 10 cm of femur were resected and replaced by a fiber titanium implant which extended over the knee joint. Autologous bone from both posterior iliac crests was added and a plaster cast cylinder applied. The cast was changed for a cast brace on June 15. X-rays in September 1976, shows bridging of the prosthesis with bone. The patient was asymptomatic and full bearing without supports. In January 1980, the patient presented with a mass in the popliteal fossa. A biopsy indicated recurrence of a giant cell tumor. Exploration of the mass revealed a soft tissue recurrence without involvement of bone. Bone in contact with the mass and related fiber metal were fixed. The patient is asymptomatic at present.

Case #4. A 32 year old male who was involved in a car accident in July 1976, where he sustained a severely comminuted compound fracture involving the distal end of this left femur. At the time of initial debridement excision of the involved 12 cm of the distal left femur was required because of marked comminution and massive contamination of the wound. The patient was then placed in skeletal traction for two weeks and a split thickness graft was used to provide complete coverage to the anterior portion of the wound. He was referred to us six weeks after his surgery for further reconstruction immobilized in a long cast. His wound was completely healed without evidence of infection. X-rays showed a complete loss of the distal 12.5 cm of the femur. Severe shortening amounting to 6 cm had occurred. After admission the cast was removed and skeletal traction was instituted. In 10 days, the original length was restored. On September 23, 1976, segmental replacement of

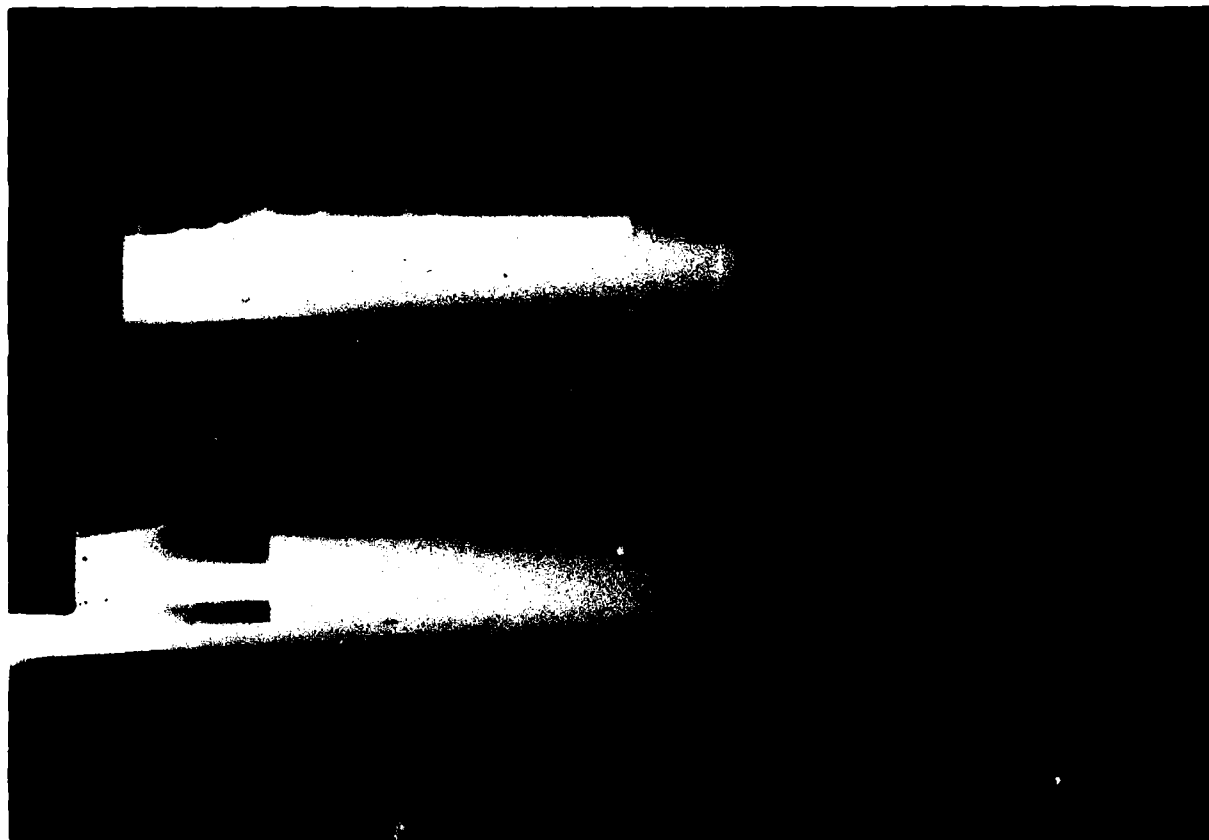


Figure 24 Composite AP and lateral
view of Case #2. 22 months
post operative.

the left distal femur with arthrodesis of the knee joint was carried out. Autologous bone grafting from both posterior iliac crests was performed. The patient did well post operatively and is at present ambulatory without supports.

Case #5. A 56 year old laborer who developed a mass in the posterior aspect of the distal right thigh in January 1971. A open biopsy was carried out by his referring physician on March 21, 1972 and he was referred to the Mayo Clinic for definitive treatment. Examination revealed a firm 4 x 2 cm movable mass in the posterior aspect of his distal right thigh. His general examination was within normal limits. Staging procedures revealed no evidence of metastatic disease. X-rays revealed a calcified irregular mass in the posterior lower right thigh. Tissue from the previous biopsy was reviewed and revealed a malignant fibrous histiocytoma. On March 27, 1972, a radical en bloc resection was performed. His post operative recovery was uneventful. More than three years later, however, the patient developed a metastatic lesion in the left upper lobe and on June 20, 1975, a thoracotomy and wedge resection of the metastatic lesion was performed. Recovery was excellent and the patient remained asymptomatic until nine months later when he returned complaining of aching discomfort in the right thigh. X-rays showed a solitary osseous lesion involving the distal right femur. Re-evaluation revealed no other evidence of metastatic disease. On March 12, 1976 an open biopsy revealed metastatic malignant fibrous histiocytoma and a segmental resection of the osseous lesion was carried out. This involved 12.5 cm of the right distal femur. The integrity of the bone was restored with a fiber metal prosthesis and iliac bone grafting. His post operative course was excellent and primary wound healing was obtained. Ten days later a cast brace was applied with polycentric knee hinges. He was dismissed from the hospital two weeks post operatively. He was then seen again six weeks later and the patient was noted to be active and had no discomfort. He had 30 degrees

of knee flexion. X-rays showed early maturation of the iliac bone grafts. At that time his cast brace was changed and he was dismissed home. Unfortunately, one month later the patient developed GI distress and died of a GI hemorrhage. No autopsy was performed.

Case #6. This 52 year old female was evaluated at the Mayo Clinic on November 22, 1977 with a six week history of an aching discomfort in her left knee. X-rays revealed a destructive lesion in the distal portion of the diaphysis of the left femur consistent with a malignant cartilage tumor. Pre operative evaluation revealed no evidence of metastatic disease. On November 23, 1977 15 cm of the distal femur were resected and replaced with an aluminum spacer. On December 23, 1977 the spacer was removed and the fiber metal prosthesis was inserted and iliac bone grafts were placed around the implant. Post operatively she was immobilized in a cast brace. She had been full weight bearing in the cast brace which was removed in August of 1978. At that time there was clinical union between the proximal distal aspects of the implant with the femur. Follow-up at 17 months post operatively showed no evidence of local recurrence of metastatic disease. She remains fully active with a cane and has only mild intermittent discomfort in the thigh. She has full extension in her knee with active flexion to 85 degrees. She has good quadricep strength. There is no tenderness. Clinically she had good stability. X-rays showed maintenance of fixation of the implant without any evidence of loosening.

Case #7. This patient is a 21 year old white female secretary who had a presumed benign tumor of her proximal left tibia excised and bone grafted by her local physician in 1977. In the fall of 1978 the lesion recurred. X-rays and histology were reviewed and a diagnosis of grade 4 osteoblastic osteosarcoma was made. Clinical staging revealed no evidence of metastatic disease. On January 16, 1979 a 13 cm section of the proximal left tibia

and associated soft tissues were removed. A titanium spacer was inserted and the leg was placed in a long leg cast. On February 13, 1979, the wound was reopened and no residual tumor was found. The titanium spacer was removed and a fiber metal prosthesis was inserted. It was elected not to use a titanium plate. Bone grafts from the ilium were placed around the fiber metal implant. On March 7, 1979, the long leg cast was removed on May 10, 1979. She was instructed to begin progressive weight bearing. When last seen on November 20, 1979, she was walking without any support. She noted no pain with weight bearing, but had mild stiffness in her knee on arising in the morning. There was no evidence of local recurrence or systemic metastasis. She walked well. Leg lengths were equal. The knee motion ranged from 0 to 140 degrees. She had good ligamentous stability. X-rays showed satisfactory consolidation of the bone grafts.

Case #8. A 31 year old female first noted left leg pain in February of 1976. Pain progressed and x-rays in October revealed a bony lesion of her left tibia. This was characteristic of a low grade cartilaginous tumor. She underwent resection of a grade I chondrosarcoma of the diaphysis of the left tibia on November 29, 1976. 16.5 cm of tibia were resected at that time. An aluminum spacer was inserted to restore the length of the bone until a special fiber metal implant was constructed. The usual titanium plate was not utilized because of the stability conferred by the intact fibular. Her post operative course was excellent. She remained ambulatory in a cast brace followed by an orthoplast splint for six months. One year later she was walking without support with minimal discomfort. She had a full range of motion in her knee and ankle. X-rays revealed a paucity of bone at the proximal end of the prosthetic device and it was elected to add more bone grafts at this

area. This was undertaken on December 2, 1977. She was last seen on June 19, 1979. There was no evidence of local recurrence of her tumor. She has a normal gait and is fully active with occasional stiffness and discomfort in the medial compartment of her knee. She has a normal range of motion in her knee and ankle. She has normal stability and alignment. X-rays showed excellent consolidation of the bone grafts.

Case #9. This is a 34 year old male factory inspector who was evaluated at the Mayo Clinic on August 29, 1979 with a three month history of discomfort in the anterior aspect of his left thigh. The discomfort was worse with activity and also bothersome at night. X-rays revealed a 9 cm lytic destructive lesion in the proximal portion of the mid shaft of the left femur with cortical thinning. Bone scan showed increased uptake at this area. No evidence of metastatic disease was detected. An open biopsy revealed a grade 4 osteosarcoma. On September 4, 1979, a radical en bloc resection was carried out involving 14.5 cm of the femur and associated soft tissues including the femoral artery. A fiber metal implant was inserted with additional fixation achieved by a 16 hole Vitallium side plate. Autogenous iliac bone grafts were applied and a reconstruction of the femoral artery carried out with saphenous vein graft. Post operatively he ambulated with crutches. When seen last on March 6, 1980, he had no evidence of local recurrence or systemic spread. He was partial weight bearing without discomfort. There was a full range of motion in his hip and knee. X-rays showed good consolidation of bone about the proximal distal ends of the implant with less bone growth about the middle portion. He was advised to continue progressive weight bearing.

Case #10. This 39 year old female was evaluated at the Mayo Clinic on July 20, 1978, with discomfort in her left hip and thigh of six months duration. The discomfort became progressive. X-rays showed a destructive lesion in the medullary

cavity of the distal shaft of the left femur. Cartilaginous calcification with endosteal scalloping and destruction were typical for a chondrosarcoma. Pre operative evaluation revealed a grade 1 chondrosarcoma. A segmental resection of 13.7 cm of the shaft of the femur was performed and a 5-1/2 inch titanium spacer inserted. Additional fixation was achieved with a 7 hole titanium plate and autogenous iliac bone grafts applied to the defect. Her post operative course was excellent and she was ambulated with a cast brace. The cast was removed four months later. When seen eight months post operatively there appeared to be good bony fixation proximally with new bone formation along the implant. However, because of deficient bone formation at the distal end of the implant on March 13, 1979 additional iliac bone grafts were applied to this area. Two loose screws at this site were removed. Five months later she was walking without support and noted no discomfort. X-rays showed considerable new bone formation distally. She had full extension with good quadricep strength but had only 10 degrees of flexion. On January 15, 1980 the titanium plate was removed and a quadriceplasty performed. Her post operative course was excellent and she was immobilized in a cast brace until March 17, 1980. At that time x-rays showed good consolidation of bone around the implant. The union at the inferior portion of the prosthesis appeared very solid. Examination under the image intensifier showed no evidence of motion. A physical therapy was instituted to mobilize and strengthen her knee.

Case #11. This 52 year old female patient had an osteosarcoma of the distal femur, and because of her refusal of an amputation, a radical resection of the distal 50% of the femur en bloc with an A-joint was carried out in December, 1978. An arthrodesis preserving the length of the extremity was done with a hip-to-ankle intramedullary rod. The deficit was filled with a fiber metal composite cylinder. Two intracalary cortical grafts were used medially and laterally from the

proximal femur to the proximal tibia. The device was then onlayed with iliac grafts. Subsequent to her procedure, she was immobilized in one-and-a-half hip spica. X-rays to date demonstrate no shift in position of the device, and what appears to be union between the cortical grafts at the femur and tibia. She is currently fully ambulatory without supports.

Discussion

The early results reported on in this paper are encouraging. Prosthetic devices made of titanium fiber composites can function in humans under weight bearing conditions. The biocompatibility appear to be satisfactory; no adverse response had been noticed clinically, radiographically, or in histologic evaluation. This confirms the experience obtained in previous animal studies. The operative procedures were comparatively simple. Good initial stability, which is believed to be important to accomplish successful bone ingrowth and bone bridging, could easily be obtained. The length of the fiber metal segment and the medullary projections are important to ensure such stability, as also the application of the plate in compression. In one patient the distal bone fragment was very small. It was felt at surgery that the plate alone might not provide adequate stability. Consequently, methylmethacrylate was used. The use of acrylic cement, however, should be avoided when possible as it prevents bone ingrowth into the intramedullary parts of the fiber composite. Animal experience has shown that bone formation into the intramedullary rod in every instance provided a crucial source of long term stability to the system. Following the experience in animals massive bone grafts from both posterior iliac crest have been used. Sufficient bone to cover the entire length of the resected segment was obtained in every instance.

One operative problem encountered was difficult to close the skin over the transplanted bone in cases where resection of the segment had been done in a previous operation. It may be necessary, as in one of our patients, to complete

bone grafting in a secondary operation. It is advantageous, if feasible, to excise the diseased bone and insert the prosthesis at the same time. When the operation is carefully planned it does not prolong the procedure unreasonably. Should for some reason the implantation of the prosthetic device be delayed, length should be retained by either inserting a temporary prosthesis, to serve as a spacer, or by the use of extrasketal fixation. In one of the patients, considerable length loss occurred and treatment of traction for 10 days was necessary to regain normal leg length.

Lesions of the distal femur and proximal tibia probably constitute the most common indications for this type of procedure. It was chosen in these patients to arthrodesse the knee joint across the fiber titanium prosthesis. Alternative procedures such as replacement with knee arthroplastics can be considered. The patients operated on so far, however, were all comparatively young and very active and the long-term results of such a procedure, therefore, in question.

Radiography and histology indicate that the bone grafts quickly consolidate around the prosthesis. The continuity of the bone is thus restored, and hopefully long-term stability is ensured and the risk of loosening minimized. Further evaluation of patients will ultimately determine the role of the procedure is reconstructive surgery.

VIII. METAL RELATED COMPATIBILITY STUDIES

A. Metal Carcinogenesis--A Study of the Carcinogenic Activity of Solid Metal Alloys in Rats

A paper by that title was authored by A. Gaechter, J. Alroy, G.B.J. Andersson, J. Galante, W. Rostoker and F. Schajowicz, was based on work done under this grant. It appeared in the Journal of Bone and Joint Surgery, Vol. 59-A:5, July, 1977, pp. 622-624. The following represents the substance of the manuscript.

Introduction

Metals, metallic alloys and polymers are being implanted in the human body with increasing frequency. It was estimated, for example, that approximately 1000 total hip arthroplasties are performed every day all over the world (42). Only a few reports described tumors associated with surgical implants in humans (40,41,45) or in animals (38,43,49). However, the introduction of new implant materials and the younger age of patients being treated raise serious concern about possible carcinogenic hazards.

Most of our knowledge concerning the possible carcinogenicity of implanted materials comes from animal studies. These studies showed that not only is the chemical reactivity of the implanted materials important but also their physical characteristics, geometry, and surface textures (39,46). Certain compounds containing beryllium, cadmium, chromium, cobalt, iron, lead, nickel, selenium, zinc and titanium appear to be carcinogenic in experimental animals (50), as do many plastics (47). However, there have been only a few animal studies of the carcinogenic hazards of the metallic alloys commonly used for surgical implants. Heath and associates induced sarcomas in rats when cobalt-chromium-molybdenum wear products from total joint-replacement prostheses were implanted in muscle, and suggested that there is need for further careful investigation into the possible hazards of such wear products (51). Other alloys are also used extensively with little knowledge of their carcinogenic potential.

The purpose of this investigation was to study the carcinogenic potential of several metallic alloys, currently in use for human implants, after implantation in muscle in rats.

Materials and Methods

Sprague-Dawley albino inbred rats (Charles River Breeding) were used for implantation. They were housed in polycarbonate cages (49.5 cm long, 26.7 cm

wide, and 16.5 cm deep) with stainless-steel tops. A maximum of three animals of the same sex were housed in each cage. Processed pine shavings (Pin-Dri Lab Products, Garfield, New Jersey) were used as bedding material. Standard food (Purina Rat Chow) and fresh water were freely available. Six months after implantation, tetracycline hydrochloride (twenty milligrams per 100 milliliters) was added to the drinking water because the animals were plagued by pulmonary infections (*Bordetella bronchiseptica*).

Each rat was labeled using an ear-punching code at the time of implantation. Daily checks were made by the attendant, and every three weeks the animals were weighed and individually evaluated. Animals that did not survive the first six months, lost their implant, or lost their earcode due to bites were excluded from the study. Of the initial 310 animals, 260 were included in the study. A two-year experimental period was planned, but rats seriously affected by tumors before that date were killed and evaluated.

Seven metal alloys (Table VI), all currently used for prostheses and internal fixation in humans, each were implanted in a separate group of rats. In addition, there were three control groups of rats: one with no surgery, one in which a sham operation was performed, and one in which Silastic was implanted.

All test coupons consisted of polished rods 1.6 millimeters in diameter and eight millimeters long, with rounded edges. The specimens were fabricated and their surfaces were polished and cleaned as required in the ASTM specifications for metallic surgical implants (37).

Each type of test coupon was implanted in the gluteal muscle mass of fifteen female and fifteen male rats except for the stainless-steel (316L) coupons, which were implanted in twenty males and twenty females. The control groups consisted of fifteen females and fifteen males. The ages of the rats at the time of surgery ranged from twenty to thirty days and the weights, from seventy-five to 150 grams.

TABLE VI

METAL IMPLANT MATERIALS

Alloy or Trade Name	Composition	Manufacturer
Stainless Steel 316 L	0.02C, 0.47 Mn, 0.01 P, 0.003 S, 0.46 Si, 17.2 Cr, 13.77 Ni, 2.46 Mo, 0.24 Cu, 0.11 Co, Bal. Fe.	Joslyn Stainless Steel Co., Indiana
Wrought Vitallium	19-20 Cr, 14-16 W, 9-11 Ni, 0.15 C max., 2 Mg max., 1 Si max., 3 Fe max., Bal Co	Howmedica, Rutherford, New Jersey
Cast Vitallium	27-30 Cr, 5-7 Mo, 2.5 Ni max., 0.2-0.3 C max., 1 Mg max., 1 Si max., 0.75 Fe max., Bal Co	Howmedica, Rutherford, New Jersey
IMI	3 Al, 8 V, 6 Cr, 4 Mo, 4 Zr, Bal Ti	Alloy Specialties, Garden Grove, California
Unalloyed titanium	0.0009 C, 0.286 Fe, 0.030 O, 0.10 N, 0.0014 H, Bal ti	Astro Metallurgical, Wooster, Ohio
MP 35N	C 0.025 max., Cr 19-21, Fe 1.0 max., Mn 0.15 max., Mo 9.5-10.5, Ni 33.0-37.0, P 0.015 max., S 0.0015 max., Si 0.15 max., Ti 0.65-1.0, Bal Co	Latrobe Steel Co., Latrobe, Pennsylvania
Titanium 6 Al-4V	0.032 C, 0.17 Fe, 6.32 Al, 4.23 V, Bal Ti	Astro Metallurgical, Wooster, Ohio

*Composition in percentages by weight.

†Analysis supplied by manufacturer.

#Specification.

Surgery was performed under general anesthesia with intraperitoneal Nembutal (pentobarbital) and the muscle and skin were closed with 4-0 chromic catgut sutures.

The animals were killed with an overdose of chloroform and complete necropsy (excluding skull and brain) was performed on all of them. All tumors seen macroscopically were photographed in situ, removed, and fixed in 10% buffered formalin. The following organs were removed routinely and processed for histological evaluation: thyroid with larynx, lung, liver, spleen, pancreas, kidney, adrenal glands and ovaries or testes. Each implant with the surrounding tissue was examined histologically. In the sham group the incised muscle was removed for histological examination.

Formalin-fixed tissues were embedded in paraffin and sections five to seven micrometers thick were prepared and stained with hematoxylin and eosin routinely, and with van Gieson, periodic acid-Schiff, and Giemsa stains when necessary for diagnostic purposes.

Roentgenograms were made of sixty animals (eighteen months old or more) selected randomly from all groups, to exclude skeletal tumors. Only masses showing neoplasia were classified as tumors. Granulation tissue from injuries, bites, and the like were classified as such. Statistical analysis was performed using the chi square test.

Results

No organ showed histological changes that could be related to a toxic effect. Tumors were found in sixty-seven of the 260 rats finally evaluated. Forty-eight rats had one or more benign tumors and nineteen had malignant tumors, twelve without and seven with metastatic lesions. The tumors without metastasis were four adenocarcinomas of the breast, three squamous-cell carcinomas, and one each of the following: adenocarcinoma of the rectum, mesothelioma, poorly

differentiated carcinoma of unknown origin, schwannoma, and rhabdomyosarcoma. The tumors with metastasis included two mesotheliomas, two instances of malignant myeloproliferative disease, and one case each of reticulum-cell sarcoma, lymphoma, and malignant histiocytoma.

Of the nineteen malignant tumors, thirteen were in animals implanted with metallic alloys, two in animals implanted with Silastic, three in the control group not operated on, and one in the sham-operation group (Table VII). Only one tumor appeared in a rat younger than fourteen months old.

There were no statistically significant differences between the incidences of tumors in each of the implant groups, in the Silastic group, and in the sham group ($p > 0.95$). There were also no differences in the incidence of tumors in males and females.

None of the tumors (malignant or benign) originated at the site of the implant, and no inflammatory reactions were observed in these areas. A delicate collagenous capsule was always found surrounding the implant and the histological pattern of this layer was comparable for the different materials.

Discussion

The results of this study show that solid implants of seven different metallic alloys commonly used in orthopedic surgery do not constitute a major carcinogenic hazard when implanted in the muscles of rats. This is an encouraging finding, but must not be taken to suggest that no carcinogenic effects can exist when the same alloys are used in humans. Clinical reports have indicated that tumors occur only after a considerable period of time (40,41,45,48). The induction time in rodents is certainly much shorter, but no evidence is available to substantiate that two years in rats corresponds to the often-quoted "thirty to fifty year latent period" for humans (49). The average life span of Sprague-

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INTERNAL PROSTHETIC REPLACEMENT OF SKELETAL SEGMENTS
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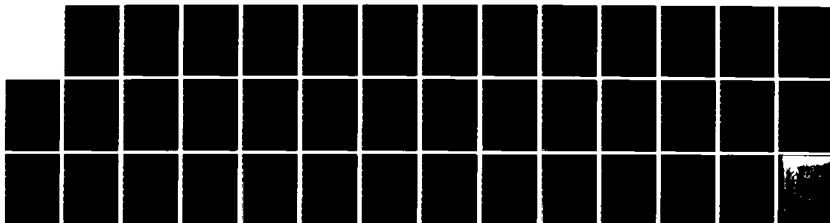
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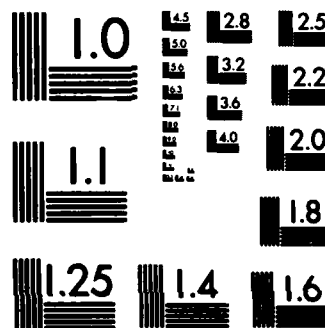
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MICROCOPY RESOLUTION TEST CHART
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TABLE VII

MALIGNANT TUMORS FOUND AT AUTOPSY

Implant Material	No. of Rats Autopsied	No. of Tumors without Metastasis	No. of Tumors with Metastasis
Stainless Steel	34	3	1
Wrought Vitallium	27	1	1
Cast Vitallium	22	-	-
RMI	22	2	-
Unalloyed Titanium	24	1	-
Ti 6 Al-4V	22	-	1
MP ₃₅ N	30	1	2
Silastic	28	1	1
No Implant	25	3	-
Sham Operation	26	-	1
Total		12	7

Dawley rats is between twenty and thirty months.

As mentioned previously, the physical characteristics of implants have been found to be important (39,46). A rod shape was chosen here since a previous study showed that rod-shaped implants cause a greater tissue reaction than disc-shaped ones (52). Human implants exist in many different shapes. Although they are usually solid when implanted, wear particles are produced which have a much larger ratio of surface area to unit mass. These particles may constitute an increased carcinogenic hazard, as suggested by Heath and co-workers and by Swanson and associates.

Muscle tissue has been used as the host for implants almost exclusively in studies of metal carcinogenesis. Bone, to which the human orthopedic implants are applied, is a biologically different tissue, which may or may not respond differently.

Clinical studies have, as a rule, disclosed corrosion in the metal implants adjacent to the tumors. Electrolytic reactions of dissimilar metals in contact are believed to have contributed greatly to the neoplastic response. Although this study cannot shed any light on that problem, it is obvious that such risks may prevail and should not be taken lightly.

Although our results must be interpreted with these reservations in mind, the outcome of this study is reassuring. Careful follow-up of clinical experiences is essential to gain further knowledge of the carcinogenic hazards of metallic implants and the induction time of tumors in humans.

B. Couple Corrosion Among Alloys for Skeletal Prostheses

A paper with this title authored by W. Rostoker, C.W. Pretzel and J.O. Galante was published in the Journal of Biomedical Materials Research, Vol. 8, pp. 407-419 (1974). It was based in part on work done under this grant. The

substance of the paper is presented as follows.

Introduction

Because of possible accelerated corrosion, prohibition against the physical or electrical contact between dissimilar metals in the design of new and improved prostheses is quite restrictive. Apart from inertness the prostheses must provide resistance to fracture under fluctuating loads. In the case of human joint replacements wear resistance at the articulating surfaces is an added major requirement. To find adequate fatigue strength, wear resistance and corrosion resistance in one material necessarily involves some compromises.

For example the fatigue strengths of heat treated titanium alloys might be expected to be higher than those of Co-Cr-Mo alloys but the wear behavior is decidedly inferior. For that reason there are prosthetic devices that use the Co-Cr-Mo alloy at the articulating surface and a titanium alloy for the weight-bearing shaft. It has been discovered (53) that a graphite-filled, ultra-high molecular weight polyethylene articulating with cast Co-Cr-Mo alloy gives improvement in the reduction of wear particle volume. Yet graphite, in principle, serves as a cathode to almost all metals to which it is coupled. The question to be resolved is to what extent the undoubtedly high corrosion potentials developed between some unlike conductive materials result in corrosion from current generated in the presence of any electrolyte typical of body fluids.

Corrosion represents a double hazard in degradation of the mechanical properties of the prostheses and in toxic responses elicited in both nearby tissue and remote organs of the human body. Corrosion fatigue is well recognized as a phenomenon although its mechanisms and post failure basis for positive identification are still vague. There is evidence (54) that stress-corrosion cracking is not induced in 316 stainless steel, Co-Cr-Mo alloy or Ti 6% Al 4% V alloy by body fluids. However, corrosion pits may be expected to act as stress concentrators

leading to fatigue crack nucleation. This hypothesis has been proposed in some published post failure analyses (55-57).

The major concern has been the discharge to the surrounding tissue of heavy metal ions, interaction with local cellular elements, and their transport to remote parts of organs of the human body. There are continuing unresolved questions as to the extent and distribution of metal ion build-up and tolerance. In a large study program using rabbits (58) it was demonstrated that, in all cases, elements of the implants occur in the surrounding tissue in concentrations significantly higher than normal. It is quite clear that tissue tolerance is a highly variable factor because in these studies titanium from titanium implants was shown to be very high in concentration but the tissue showed no abnormal features.

The presence of an implanted prosthesis can be monitored in humans by analysis of blood, urine and hair. Thus, for example, it is claimed that the use of metal-to-metal hip joint prostheses can lead to cobalt concentrations higher by a factor of 10-20 whereas metal-to-polymer prostheses gave no detectable increase over normal (59).

The patient himself can provide indication of corrosion activity. There are several papers which relate that patients have experienced pain and localized inflammation (55,57,58,60) necessitating removal of an implant. The recovered prosthesis was sometimes undamaged except for evidence of localized corrosion.

The surrounding tissue can provide an indication of unusual corrosion activity by simple discoloration (59,61-63), reddish in the case of stainless and other steels and blackish in the case of Co-Cr-Mo alloy and titanium alloys. There are histological indications of the effects of corrosion products (62,62) necrotic tissue, granuloma formation, foreign body giant cells, and polymorphonuclear leukocytes.

Evidence of malignant responses exist (58,59,52) but their clear correlation to generation of corrosion products is not substantial.

There is a large body of relevant published literature describing the incidence and evidences of corrosion by prosthetic materials implanted both in humans and in animals. Apart from inappropriate usage of carbone steel and commercial ferritic stainless steels, prosthetic and other implanted devices are manufactured from austenitic steels, the cast Co-Cr-Mo alloy, the wrought Co-Cr-W-Ni alloy, titanium alloy 6% Al 4% V and MP35N (which is a Co-Ni-Cr-Mo alloy). All of these materials possess a passive film in saline solutions with neutral pH. It is generally observed (54,55,64) that corrosion when it occurs is of the pitting type.

By far the highest proportion of instances where corrosion in an implanted object has been identified are associated with the austenitic stainless steels (56,60,64-66). On the basis of a very large survey (60), it was reported that none of the implants made from Co-Cr-Mo alloy had to be removed for reasons of corrosion-induced pain or inflammation. There are three recorded and documented cases in which Co-Cr-Mo devices (61,66) and a Co-Cr-W-Ni device (57) had to be removed for reasons which were subsequently ascribed to corrosion.

In almost all instances (56,60,64-66) corrosion is located at the interface between a screw and a plate. In some papers this is referred to as "face" corrosion. Face corrosion is properly identified as a form of crevice corrosion or fretting corrosion or a combination (64,65,67). Relative motion and abrasion between screw and plate is always possible and unless the passive film repairs itself rapidly, accelerated production of corrosion products can be expected. Relatively anaerobic conditions can also be expected in this same region so that either mechanism or both can be assumed.

Although the hazard of couple corrosion has been ascribed to the use of

two different types of stainless steels in a device, there is significant evidence (60,65,68) that under such circumstances abnormal or more frequent corrosion does not occur. Thus, according to Scales, et al. (60), the use of 304 or 303 screws with 316 plates or vice versa did not increase the frequency or face corrosion over that encountered with plates and screws of the same grade of stainless steel.

In vitro studies of the corrosion of prosthetic alloys (69-72) have contributed significantly to our understanding of their behavior. When alloy specimens are immersed in neutral saline or physiologically equivalent solutions they are initially corrosion active but their potential with respect to a reference cell drops over a period of time and slowly approaches a stable value called the "rest potential". Presumably during this period the passive film is developing.

The stability of the passive film may be assessed by measuring the corrosion current density as a function of potentiostatically applied voltages. At some established voltage the corrosion current increases abruptly by at least two orders of magnitude (69) and concurrently corrosion in the manner of pit formation is observed (69-71). One can compare the stabilities of the passive films of alloys by the differences between the rest potentials and the breakdown potentials. This difference increases in the order of arrangement: 316 stainless steel, Co-Cr-Mo alloy, and titanium (69,71,72) which agrees with general impressions of the relative corrosion resistance of these materials.

In vitro corrosion rates under passive conditions are finite and measurable. They appear to be the same for all three materials; placed at $0.5 \mu\text{A}/\text{cm}^2$ by Mueller and Green (71), but decreasing with time to less than $0.015 \mu\text{A}/\text{cm}^2$ as indicated by Revie and Greene (70). Furthermore, in vitro corrosion rates have been placed (70) at only about one-tenth of the in vivo corrosion rates. If one accepts the

$0.015 \mu/\text{cm}^2$ as the long-term rate in vitro, converted to in vivo rates provides for about 5.4×10^{-2} mils/year in terms of stainless steel. Although the basis is not made clear, Greene and Jones state that 1×10^{-2} mils/year is tolerable for surgical implants.

The efficiency of aeration is seen to be a major factor in the stability of the passive film (71) since it is shown that in changing from deaerated to strongly aerated solutions the breakdown potential increases from 0.4 to 0.8 V (hydrogen reference). This is in concert with the evidence that the crevices (i.e., low oxygen concentration) are most conducive to breakdown of corrosion resistance.

If one examines the differences between the measured rest potentials and breakdown potentials for these materials, it seems reasonable to conclude that the cell potential of one of the metals against the oxygen reduction reaction is more likely to overcome a breakdown potential than the cell potentials developed between combinations of these metals (69).

Scope and Procedure

The following materials, from the viewpoint of combinations of corrosion resistance, strength and/or wear resistance, can be considered as candidates for design of implanted prostheses:

stainless steel 316L	ASTM F55-66 (10/14% Ni, 16/18% Cr, 2/3% Mo)
cast Co-Cr-Mo alloy	ASTM F75-67 (27/30% Cr, 5/7% Mo, 0.20/0.35 max% C)
wrought Co-Cr-W alloy	ASTM F90-68 (19/21% Cr, 14/15% W, 9/11% Ni, 0.15 max% C)
Ti-6% Al-4% V	ASTM B367-69 Grade CS
Multiphase-MP35N	Tradename of wrought high strength alloy produced by Latrobe Steel Co. Nominally: (35% Co, 35% Ni, 20% Cr, 10% Mo)
Graphite	

The objective of the study was to create and conduct an in vitro corrosion test that would indicate for or against increased hazard of corrosion when combinations of these materials were in physical contact. On the basis of the in vivo and in vitro published studies reviewed, it was decided that a crevice condition was most conducive for these materials to corrode. The literature also is clear that corrosion when it initiates and follows a pitting mode.

Pitting can be readily identified and measured on polished surfaces. By relatively simple optical techniques the number of pits per unit area, their diameters and depths can be measured. Deposits and stains produced by corrosion products generate sharp contrasts against a light-reflective background.

Aspecimen design which simulated both a "couple" and a crevice condition is illustrated. The two contacting surfaces were polished to a metallographic quality of finish. The smaller diameter specimen was about 1/2 in. diameter; the larger diameter specimen was about 1 in. diameter. The central hole through which the nylon bolt was inserted was 0.170 in. diameter. Each assembly was immersed in a separate wide-mouth open, 32 oz. jar containing 1% saline solution prepared from reagent grade sodium chloride and distilled water. Large numbers of jars with their individual specimens were held in a water bath to $37 \pm 0.5^{\circ}\text{C}$. The saline solution level was kept constant by replenishing additions of distilled water.

After the planned exposure time the specimens were disassembled, rinsed and dried preparatory to examination by optical microscope at magnifications ranging from x50 to x1000. Examination was over the whole polished surface. Exposure times ranged from a few days to as much as 100 days. Each exposure was uninterrupted by intervening examinations.

A method was developed for mechanically rupturing the passive film while immersed in the test solution in order to evaluate the ability of a metal to rejuvenate

its corrosion-protective film. A series of burrs were created by diamond pyramid hardness indentations made along a radial line into the polished surface. The raised metal around the indentation served as an abrasive or cutting edge on the opposing surface. The indentation also generates local cold work and an embryo pit configuration. Only one member of a couple was indented. Such specimen assemblies as in Figure 25 were immersed in 37°C saline solution for one week to establish the oxygen depletion in the crevice. The jar, fluid and specimen were transferred to a larger container where manual manipulation was possible. In the large container the specimens were twisted relative to each other producing short circumferential scratches in the nonindented specimen. The assembly otherwise undisturbed is then transferred back to the 32 oz. wide-mouth jar and the thermostatic bath. During all of this procedure the assembly is sustained and continuously immersed under saline solution. Surfaces were examined after 100 days of immersion.

Preliminary Observations

A crevice condition is created simply by bolting together two polished surfaces of 316L stainless steel. Pitting corrosion was obvious after as little as five days of exposure to 37°C saline solution. The products of pitting corrosion appear as a red stain outside of the region of the crevice. Presumably the corrosion products remain in ionic form until by diffusion they reach an electrolyte richer in dissolved oxygen--at which point they form the insoluble, rust-red precipitate.

The dimensions of pits could be measured readily at x100 magnification. The pits were observed to be cone-shaped volumes of approximate dimensions: 3×10^{-4} in. diameter at the surface and 5×10^{-3} in. deep. Smaller pits were not observed even at higher magnifications. The depth of a pit was measured using a microscope with a calibrated focusing rank. The height difference in

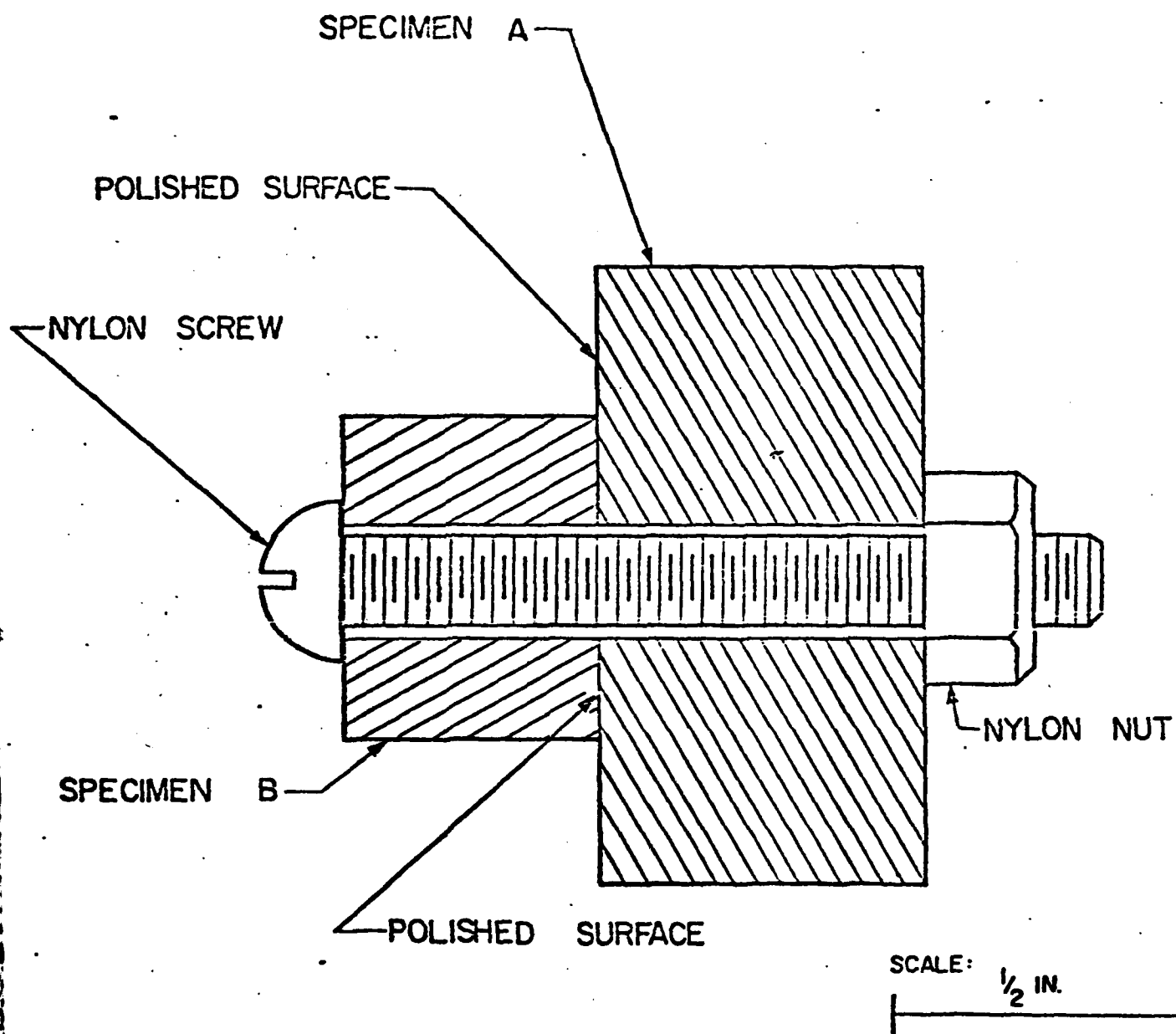


Figure 25

Diagram of corrosion
specimen couple.

the focusing position from the surface immediately around the pit and the bottom of the pit corresponds to the pit depth. The volume of such a pit is about 5.3×10^{-10} in.³. For purposes of comparison with the literature on corrosion tolerance (70), the recognition of one pit on a 1/2 in. diameter surface after a 100-day exposure corresponds to a corrosion rate resolution of about 1×10^{-5} mils/year. This procedure for estimating corrosion rates is reasonably valid for well separated pit populations. With a high population of pits the deposits of insoluble corrosion products become an obscuring factor.

Pitting in 316L stainless steel can be generated in a crevice configuration in as little as 5 days. An uncoupled, open-faced, polished specimen of the same material will evidence pits and rusting after about 50 days. By comparison with observations of implanted prostheses the occurrence of pitting in 50 days should be taken as evidence that the conditions of the in vitro experiments are substantially more severe. Hip prostheses which had been removed because of fatigue failures after more than one year of implantation showed no evidence of pitting or rust stains (74). These observations support the contention (70) that in vivo corrosion rates are only about one-tenth of in vitro corrosion rates.

Summary of Observations

The experimental program represents one specimen or large area of each combination. The appearances of polished surfaces subjected to corrosion conditions in various configurations are described in Tables VIII to XI. Very small indications of local corrosion in a large sample area can be readily identified.

Quite clearly the susceptibility of 316L stainless steel to pitting corrosion in a crevice configuration as repeatedly remarked in the literature is verified by these experiments. These results indicate also that the tendency toward pitting corrosion is not exacerbated by coupling with other corrosion

TABLE VIII

SUMMARY OF CORROSION OBSERVATIONS ON 316L STAINLESS STEEL

<u>Configuration</u>	<u>Observations on Stainless Steel Component</u>
Uncoupled	Multiple pitting and staining (rust colored) after 50 days.
Coupled with itself (simple crevice)	Multiple pitting and staining after 10 days*
Coupled with graphite	Multiple pitting and staining after 10 days*
Coupled with Ti-6% Al-4% V	Multiple pitting and staining after 10 days*
Coupled with cast Co-Cr-Mo	Multiple pitting and staining after 10 days*
Coupled with Multiphase	Multiple pitting and staining after 10 days*

*Differences in intensity of pitting are not distinguishable

TABLE IX

SUMMARY OF CORROSION OBSERVATIONS ON CAST CO-CR-MO ALLOY

<u>Configuration</u>	<u>Observations on Co-Cr-Mo Component</u>
Uncoupled	No corrosion* after 74 days
Coupled with itself (simple crevice)	No corrosion after 100 days
Coupled with 316L	No corrosion. Polished surface heavily stained with corrosion product of stainless steel
Coupled with wrought Co-Cr-W	No corrosion after 100 days
Coupled with Ti-6% Al-4% V	No corrosion after 100 days
Coupled with graphite	No corrosion after 100 days
Coupled with Multiphase	No corrosion after 100 days

*"No corrosion" signifies that no pits were observed and that the quality of the surface was indistinguishable from the initial condition.

TABLE X

SUMMARY OF CORROSION OBSERVATIONS ON Ti-6% Al-4% V Alloy

<u>Configuration</u>	<u>Observations on Ti-6% Al-4% V Component</u>
Uncoupled	No corrosion after 74 days
Coupled with itself (simple crevice)	No corrosion after 100 days
Coupled with 316L	No corrosion. Polished surface heavily stained with corrosion product of stain- less steel
Coupled with cast Co-Cr-Mo	No corrosion after 100 days
Coupled with graphite	No corrosion after 100 days
Coupled with Multiphase	No corrosion after 100 days

TABLE XI

SUMMARY OF CORROSION OBSERVATIONS ON "MULTIPHASE" ALLOY

<u>Configuration</u>	<u>Observations on Multiphase Component</u>
Uncoupled	No corrosion after 74 days
Coupled with itself (simple crevice)	No corrosion after 100 days
Coupled with 316L	No corrosion. Polished surface heavily stained with corrosion product of stainless steel
Coupled with cast Co-Cr-Mo	No corrosion after 100 days
Coupled with Ti-6% Al-4% V	No corrosion after 100 days
Coupled with graphite	No corrosion after 100 days

resistance metals or graphite.

The cast Co-Cr-Mo alloy is much more resistant to pitting corrosion than stainless steels. In the absence of mechanical rupture of the passive film no pitting in any configuration was observed. Taking the results at face value the time to induce pitting in Co-Cr-Mo alloys is more than ten times that to accomplish the same in 316L stainless steel.

Coupling with other corrosion resistant metals or graphite did not induce pitting. Coupling the wrought Co-Cr-W-Ni alloy with the cast Co-Cr-Mo alloy did not induce pitting.

The Ti-6% Al-4% V alloy and the multiphase-MP35N alloy showed no pitting in a crevice condition and in crevice-coupled conditions.

Table XII compiles observations of changes in surface appearance resulting from mechanical rupture of the passive films while immersed in the corrosion environment. The titanium alloy seems well able to repair a ruptured passive film. However, in some instances opaque films were seen to generate at the indentation burr or at the scratches in the polished surfaces of Co-Cr-Mo and multiphase-MP35N. These were not seen at all scratch and burr locations and they did not appear to be associated with pits of finite depth. They appeared to be films which had thickened to a point of opacity to visible light.

Conclusions

These experiments indicate that, provided the passive film is not perforated, metals of superior corrosion resistance can be combined in prosthesis design to provide superior mechanical performance. Thus combinations among: Ti-6% Al-4% V, cast Co-Cr-Mo, wrought Co-Cr-W-Ni, and wrought Co-Ni-Cr-Mo alloys--all of which are presently in use--may not create a corrosion problem. Such designs must provide for complete immobilization of the components; thus, plates and screws are precluded. To fully support this conclusion long term

TABLE XII

INFLUENCE OF PASSIVE FILM DISRUPTION (INDENTATION AND SCRATCHES)
ON CORROSION IN A CREVICE CONFIGURATION

Scratched Surface	Ti-6% Al-4% V	Indented Surface Cast Co-Cr-Mo	Multiphase
Ti-6% Al-4% no corrosion after 100 days	No corrosion after 100 days	Corrosion film at indentation burrs after 100 days	Corrosion film at indentation burrs after 100 days
Cast Co-Cr-Mo no corrosion after 100 days	No corrosion after 100 days	Corrosion film at indentation burrs after 100 days	No corrosion after 100 days
Wrought Co-Cr-W no corrosion after 100 days	-	No corrosion after 100 days	-
Multiphase corrosion film on scratches after 100 days when coupled with Ti-6% Al-4% V	No corrosion after 100 days	No corrosion after 100 days	No corrosion after 100 days

in vivo implant studies are needed.

The duration of corrosion inaction might be approximated from the following considerations. Evidences of "face" corrosion have shown up according to reports several months after implantation (assume 100 days). Face corrosion could be construed as crevice corrosion unassisted by fretting. In vitro crevice corrosion by the present experiments can be developed in as little as 5 days. We suppose therefore that the in vitro corrosion test represents an acceleration by at least a factor of 20. Certain crevice-coupled configurations in vitro have not produced any evidence of corrosion in 100 days. One might assume that the same configuration would be inactive as implanted for at least 6 years. If by proper design the crevice condition were eliminated, then bimetallic prostheses could be corrosion inactive for much longer.

Graphite, provided that abrasive inclusions are absent, should be allowable in contact with these alloys. Stainless steel of the 316L grade cannot be considered corrosion resistant in any configuration that simulates a crevice.

The present experiments demonstrates that the passive film can repair itself in isolated acts of mechanical perforation. However, the time of reformation has not been measured and it is likely that repeated perforation as in a sustained abrasive action might damage the corrosion resistance of any alloy in any state of coupling.

C. Anodic Polarization of Porous Fiber Metals

This is the title of a paper authored by E.P. Lautenschlager, N. Sarkar, A. Acharya, J. Galante and W. Rostoker which appeared in the Journal of Biomedical Materials Research, Vol. 8, pp. 189-191 (1974). It represents a collaboration with the first authors who are at Northwestern University. The substance of the paper is as follows.

A variety of open-pore materials (including powder metals (5), ceramics (7)

and polymers (75) have been suggested for implantable prostheses which would become affixed via soft and hard tissue ingrowth. Amongst the more innovative of these materials are the fiber metal composites (3). By compacting and vacuum sintering short, kinked fibers of metals of excellent corrosion resistance and known biocompatibility specimens displaying controlled, inter-connecting porosity as well as reduced elastic modulus, increased damping capacity, adequate strength and high resistance to crack propagation can be produced.

The purpose of the present investigation is to determine if the high degree of electrochemical stability of the bulk materials are in any way altered when fabricated into fiber metal composites.

Electrochemical techniques of corrosion-potential measurement and potentiostatic anodic polarization have been well documented (70,76,72,73). These methods were used on both fiber and bulk specimens of pure titanium and on specimens of a Co-Cr alloy of composition similar to that employed in orthopedic surgical implants. The fiber composites were 50% of the bulk densities. All specimens were 1.30 cm in diameter by approximately 1.1 cm high. The bulk specimens were heat treated an equivalent amount to the sintering time and temperature of the fiber specimen.

Specimens were lowered into Ringer's solution and the corrosion potential developed by the metal was measured with respect to the standard calomel electrode (SCE) and recorded as a function of time. During the first hour this potential became stabilized as the metal spontaneously passivated. The one hour corrosion-potentials are shown as the initial point at the top of the curves of the figure. At the one hour stabilized potential, anodic polarization was begun by increasing the potential of the specimen in steps of 50 mv of increasing oxidizing power and recording the currents necessary to maintain that

potential. Those currents, normalized by dividing by the outer surface area ($\sim 7.10 \text{ cm}^2$) of the specimen are plotted as current densities versus the potential in Figure 26.

A second set of fibrous specimens was masked by covering the surface with wax so that only the bottom circular base was exposed to the electrolyte. The current data was divided by the reduced exposed outer surface ($\sim 1.30 \text{ cm}^2$) and the resulting current densities plotted on the figure as wax covered fibrous material.

Passivity on an anodic polarization curve is indicated by little or no increase in the current density as the potential is increased (i.e., data should remain near the left side of the Figure).

In both the case of the Ti and the Co-Cr alloy the figure shows that at all potential the fiber composites exhibit higher current (i.e., more ions released from the metal into the electrolyte) than the bulk material with the same outer surface area; however, the curves of a given species are essentially parallel. This latter result indicates that the electrochemical behavior of those metals are not basically altered by the fabrication procedure. Rather, the higher electrochemical currents arise in the fiber composites from the electrolyte actually being exposed to greatly increased surface areas created by the interconnecting porosity. As the penetration of the electrolyte to this porosity is reduced (by wax or perhaps by tissue ingrowth) the anodic polarization curves tend to revert to the bulk material values.

D. Evaluation of Couple/Crevice Corrosion by Prosthetic Alloys Under in vivo Conditions

This paper by W. Rostoker, J. Galante and P. Lereim was published in the Journal of Biomedical Materials Research, Vol. 12, pp. 823-829 (1978). This

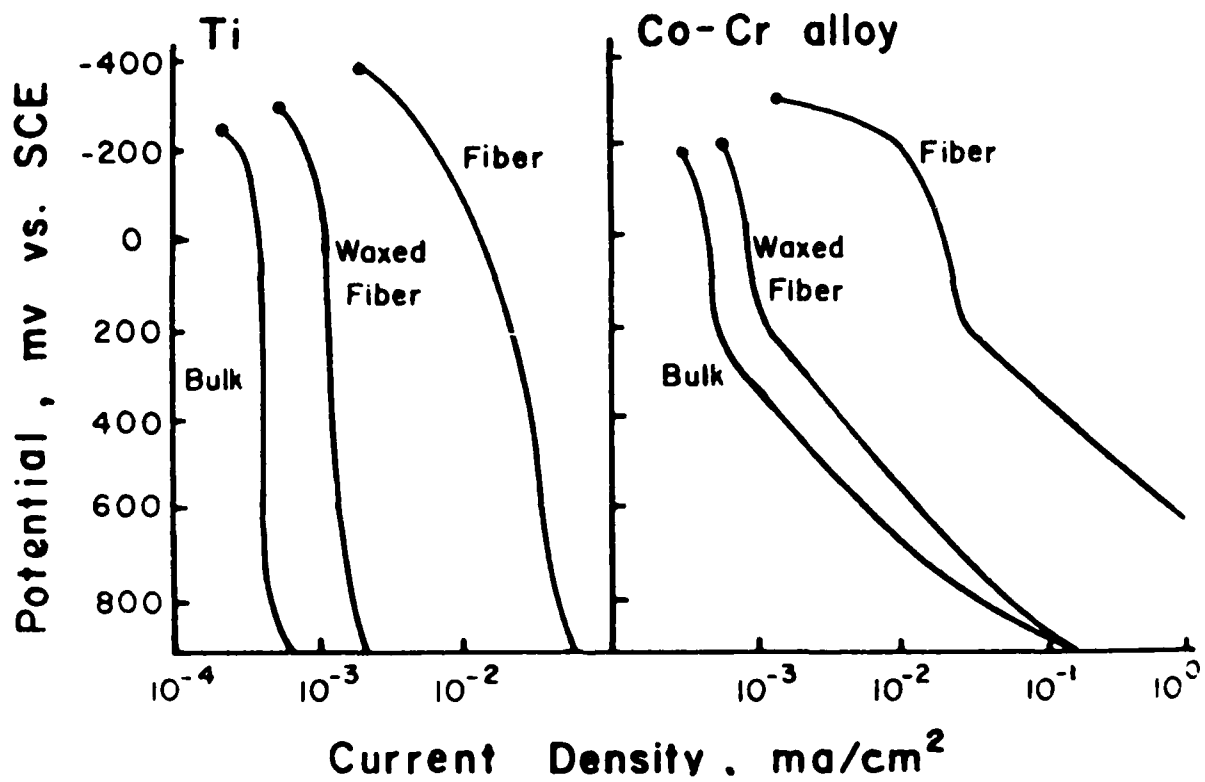


Figure 26

Anodic polarization curves
for bulk metal and fiber
composites in Ringer's
solution.

work was done in part under this grant. The following represents the substance of the paper.

Introduction

It has been stated recently (77-79) that some of the corrosion resistant alloys used in internal prostheses could be applied in composite configurations despite the proscription against the use of dissimilar metals and alloys. The existence of chemically resistant, structurally stable, high electrical resistivity films should keep corrosion currents to the level of those associated with the condition of passivity despite the existence of couple potentials. In practice a combined hazard of couple and crevice corrosion might be created at opposing interfaces by use of dissimilar passive alloys. In a preliminary evaluation (77) of the possibilities of accelerated corrosion by couple/crevice conditions in an in vitro experiment design it was demonstrated that only stainless steel 316L exhibited significant accelerated corrosion response. Stainless steel is vulnerable to crevice corrosion whether or not a couple with another passive alloy exists. The cast Co-Cr, wrought Co-Cr, Ti-6% Al-4% V and the wrought Co-Ni-Cr (MP35N) alloys were shown not to develop corrosion pits. The present paper describes the results of a similar experimental approach adapted to in vivo conditions.

Materials and Methods

Five materials were involved in selected couples: cast Co-Cr-Mo alloy (ASTM F75-67), wrought Co-Cr-W alloy (ASTM F90-68), Ti-6% Al-4% V ELI grade (ASTM B 367-69 grade CS), wrought Co-Ni-Cr-Mo alloy (Trade name MP35N), and a high purity, petroleum-coke-derived graphite. A couple/crevice specimen was created in the following manner. Thin discs of specimen material about 12 mm diameter by 3 mm thick with a 5 mm center hole were polished on one flat surface

to a quality of finish appropriate for metallographic examination. These surfaces had a mirror-like quality free of pits but not necessarily free of shrinkage porosity. The polished surfaces of two materials were clamped opposite each other by means of an acrylic rivet through the center holes. By microscopic evaluation the separation between surfaces was about 30 microns although in the practical limits of preserving flatness this must have been somewhat variable.

Four couple/crevice specimens of each of the following were prepared: cast Co-Cr-Mo/wrought Co-Cr-W; cast Co-Cr-Mo/MP35N; cast Co-Cr-Mo/graphite and cast Co-Cr-Mo/Ti-6% Al-4% V. All sixteen specimens were implanted in the paravertebral muscles of a large dog. The dog was sacrificed 30 months later. The implants were all hosted in one animal because the primary purpose of the experiment was to look for corrosion evidences on metallic specimens in a single characteristic environment. The presence of multiple implants separated from each other could not have produced an interactive effect in the corrosion processes.

At sacrifice a block of soft tissue containing each implant was removed, fixed in 6% glutaraldehyde and stored in 50% alcohol for two days until the implants were extracted. The tissue immediate to the implant was examined visually for gross changes and discoloration.

For histological examination samples were embedded in paraffin, cut into six micron thick sections and stained with hematoxylin eosin. Six sections were obtained from each specimen.

The following features were evaluated by microscopic examination:

- (a) The fibrous membrane--the thickness of this structure was measured using a Zeiss measuring eyepiece at four different points and the average values were calculated.
- (b) The cellular pattern in the fibrous layer and surroundings, the presence of inflammatory cells, blood vessels and polymorphonuclear cells were recorded.

- (c) Screening for signs of degeneration, tissue necrosis and signs of chronic inflammation.

A numerical system was used to grade the observation from 0 to 2 in increasing degree of severity.

The implants themselves were disassembled by dissolving the acrylic rivet with acetone and separating the two halves. After this process the previously polished surfaces possess a semiopaque film which disappeared after immersion in acetone overnight. Some white areas of film remained on a few specimens. These dissolved in 30% hydrogen peroxide during a 24-hour immersion; from which one may deduce that they were probably tissue ingrowths from the periphery of the crevice. The residual surfaces were examined without further treatment or preparation using a low power stereoptic, light microscope and a scanning electron microscope (SEM) looking for pitting and other evidences of corrosion.

Results

All surfaces of cast Co-Cr and wrought Co-Cr in apposition for 30 months were seen to be bright, free of tarnish films and free of corrosion pits (as distinct from shrinkage porosity). All surfaces of cast Co-Cr and MP35N in apposition were also bright, free of tarnish films and free of corrosion pits. The surfaces of the cast Co-Cr alloy in apposition to graphite was bright, free of tarnish and corrosion pits. The surfaces of cast Co-Cr specimens in apposition to the Ti-6% Al-4% V alloy were bright, free of tarnish and corrosion pits. However, the titanium alloy surfaces were lightly tarnished as seen both by light optics and electron optics.

At autopsy there were no macroscopic signs of infection or inflammation. In one sample of group I and in two samples of group II slight rust coloration of the membrane was found (see Table XIII). In two samples of group IV extensive to moderate rust color was found. One sample of group III showed blackening but

this was attributed to the low abrasive resistance of graphite.

Microscopic examination showed a fibrous tissue layer adjacent to the implant. Thicknesses varied considerably (see Table XIII) with averages: 100 microns (group I), 203 microns (group II), 154 microns (group III) and 300 microns (group IV). Note that the most extensive pigmentation corresponds to the thickest fibrous tissue layer.

No signs of acute inflammation were seen in any of the samples but those of group IV did show increased vascularity. In two of these same samples of group IV membrane cellularity was seen--a proliferation of macrophages and fibroblasts. There were no evidences of giant cells.

On examination of the organs, heart worms were found in the lungs. The lungs also gave evidence of bronchitis. There was also histological signs of hepatitis and elongated eosinophilic crystals (intranuclear inclusion bodies) in the liver. None of these indications are thought to be relevant to the generation of corrosion products.

Discussion and Summary

Cast cobalt-chromium, wrought cobalt-chromium alloys and the Co-Ni-Cr-Mo (MP35N) alloy implanted for 30 months in the tissues of a living animal when part of certain couple/crevice configurations showed no evidence of corrosion. These findings are in agreement with in vitro studies reported previously (1).

The titanium alloy, T-6% Al-4% V when coupled with the cast Co-Cr alloy showed a tarnish film which was not observed by the in vitro experiments. The existence of the tarnish film which indicates some level of corrosion activity correlated with increased average fibrous membrane thickness, cellularity immediate to the membrane and minor indications of inflammation.

These indications suggest that a prosthetic device which is a composite

TABLE XIII

OBSERVATIONS ON TISSUE IMMEDIATE TO THE IMPLANTS

GROUP NO.	SPECIMEN NO.	MACROSCOPIC DISCOLORATION	THICKNESS OF FIBROUS LAYER MICRONS (AV.)	MEMBRANE CELLULARITY	INFLAMMATORY RESPONSE	MICROSC. PIGMENTATION OF FIBROUS LAYER
I	1		50	0	0	
	2		37	0	0	
	3		126	1	0	
	4	+	120	1	0	
II	5	+	178	1	1	+
	6		135	0	0	+
	7	+	342	0	0	+
	8		155			
III	9		24	0	0	
	10	+	78	0	0	
	11		148		0	
	12		148	1	1	
IV	13	+	360	0	2	+
	14		296	1	2	
	15		453	2	2	
	16	+	259	0	0	+

of the cast Co-Cr and Ti-6% Al-4% V alloys may be inappropriate. This can only be a tentative conclusion because these experiments do not represent a full scale biological assay with adequate reproducibility and controls. These reported observations also suggest that in vitro studies alone are not completely definitive.

CONCLUSIONS

1. A porous metallic site was manufactured by molding and sintering short length metal fibers. A 50% density was used throughout an experiment with interconnecting porosity of the type required to insure bone ingrowth. These composites have unique elastic properties and exhibit large histeresis. This compliance capability is of great value in facilitating fixation during the implantation procedure and in eliminating the possibility of significant stress concentration following the application of in vivo loads.

2. A variety of prosthetic components can be manufactured using this fiber metal composite as a porous coating. Complex assemblies including segmental replacements for the tibia, femur and humerus of the adult baboons were successfully produced. Prostheses replacing major segments of the bone, such as the femur and an intervening joint such as the hip or the bone were also designed, manufactured and implanted.

3. A series of surgical techniques was developed to facilitate the precise implantation of these devices in the baboon experimental model.

4. The results of these studies indicated that with an extraperiosteal resection, the addition of a bone graft and the accomplishment of rigid fixation and intimate contact at the interfaces resulted in union and successful reconstruction of the limb in a high number of animals in a reproducible manner. The most reliable site for bone ingrowth was at the level of the intramedullary portion of the implants where union and bone ingrowth was present in 93% of the instances. Union at the interface between the end of the bone and the segmental replacement was present in 77% of the extra-periosteally grafted segments and uninterrupted bone formation across the replaced segment was present in 69% on the same group of animals.

A retrospective analysis of the non-unions indicated inadequate grafting or lack of adequate initial fixation and/or the presence of large gaps at the interface between the resected bone end and the replacement segment.

5. Long term histological evaluation indicated that the ingrown bone was viable, without any evidence of extensive bone resorption or abnormal cellular formation. No cell layer could be detected between the ingrown bony trabeculae and the titanium fibers.

6. There were no histological changes in all of the organs examined at autopsy.

7. A war casualty model was created where a contaminated wound was created with a massive loss of the tibia. Of the three animals operated on, two accomplished successful union and reconstruction of the limb without persisting infection.

8. A comparison of bone ingrowth and remodelling was made between fiber metal composites manufactured with two different pore sizes, one of 300 microns and the second one of 600 microns. The baboon femur model was used. No significant differences were found between the two groups.

9. A comparison between bone grafts of two different particle sizes bridging a diaphyseal defect was made. In one group chips of bone with large particle size was used and in other one ground bone with smaller particles was used. Marked difference between the two groups was observed. In the ground bone specimens ingrowth occurred over the total surface area and bone penetrated deep into the composite. With a larger particle size bone ingrowth was irregular and superficial.

10. A comparison between intramedullary fixation at the distal and proximal ends of the replacement segment using acrylic cement in one case and fiber titanium composite in the other was made. Complete bone bridging

occurred in all cases but fixation appeared to be more secure due to ingrowth into the intramedullary rod in the non-cemented specimens.

11. The preceding results were used as a basis for the development of a segmental replacement to be used in the reconstruction in limbs of patients who required major resection of long bones either by tumors or trauma. Twelve patients underwent surgery at the time of this report. At this time all patients are ambulatory and full weight bearing. There has been one persisting non-union that required repeated grafting procedures and one persistent deep wound infection that may require eventual removal of the implant.

12. The carcinogenic potential of solid metallic implant materials was tested in the muscle of Sprague-Dawley albino inbred rats. Conclusions indicated that no significant differences were present between the incidence of tumors in the animals with metallic implants and those in the control and sham groups. Solid implants of the commonly used metallic alloys including stainless steel 316L, wrought Vitallium, cast Vitallium, unalloyed titanium, MP35N, Ti6Al4V, and RMI titanium alloy do not constitute a major carcinogenic hazard in the muscles of rats.

13. A combination of Ti6Al4V, cast cobalt-chrome, wrought cobalt-chrome and wrought cobalt-nickel chromium molybdenum alloys were studied for their potential for crevice corrosion in vitro. These combinations did not appear to have the potential to create a corrosion problem. Anodic polarization studies of titanium and cobalt-chrome fiber composites indicated that the electrochemical behavior of these materials was not basically altered by the fabrication procedure.

14. In vivo studies of couple corrosion between cast-cobalt chromium, wrought cobalt chromium, cobalt-nickel and chromium molybdenum, MP35N and

Ti6Al4V were performed. The couples formed between Ti6Al4V and cast cobalt-chrome alloys showed the presence of some level of corrosion activity which correlated with changes in the surrounding tissues. Prosthetic devices which are a composite of cast cobalt-chrome and Ti6Al4V may be inappropriate. This tentative conclusion should be confirmed by a full-scale biological assay.

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